

Complementary and Alternative Therapy (CAM) in the Treatment of Allergic Rhinitis

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Abstract CAM is any therapeutic intervention that exists outside traditional allopathic medicine. The utilization in the US population is increasing up to 4 out of 10 patients in some surveys [1]. Given this increasing prevalence, it is essential that clinicians have the resources to advise their patients in the utilizations, benefits, and potential harms of these alternative therapies. Recent literature was reviewed in regard to traditional Chinese medicine [TCM], acupuncture, homeopathy, and herbal therapy in the treatment of allergic rhinitis limited to randomized controlled trials. Several complementary treatment studies demonstrated statistically significant benefits to patients' quality of life and symptom scoring without providing duration of effect. Alternative therapy studies have revealed mixed results in regard to efficacy. Although the adverse effect profile is low, additional studies will be required to further promote integration into the standard of care for the routine treatment of allergic rhinitis.

Keywords Allergic rhinitis · Complementary treatment · Herbal treatment · Traditional Chinese medicine · Acupuncture · Homeopathy

Introduction

Complementary and alternative medical interventions utilize techniques and devices that are presently outside the realm of

the standard care for patients with allergic rhinitis. The popularity in the US population has increased to as many as 4 out of 10 patients within the last year in some surveys [1] while complementary and alternative therapy (CAM) is more commonly used by 80 % of the world's population. Allergic rhinitis is a prevalent condition in the USA affecting 20 % of the population resulting in significant reduction in quality of life. Many patients suffering from the symptoms of allergic rhinitis have turned to CAM as an alternative to or complementing traditional standard medicine for relief. These numbers are further increasing as a result of a five times increase in the utilization of CAM in the children of patients already on CAM therapies [1].

Methods

A literature search was performed utilizing key words combining rhinitis and individually with acupuncture, traditional Chinese medicine, homeopathy, and alternative therapy. Randomized control trials were reviewed in regard to their impact on symptom scores and objective equivalents (Table 1).

TCM

In China, traditional Chinese medicine [TCM] has existed for centuries and is currently utilized by a large portion of the population. The basis of TCM is harmonization of Ying and Yang through the balancing of the elements of the body [2]. A meta-analysis by Wang et al. reviewed several studies and compiled 533 patients investigating the utilization of TCM for allergic rhinitis. They uncovered a reduction in the total nasal symptom scores [$P=0.003$] and a trend toward reduction in IgE levels [$P=0.19$] over a 3-month period [3].

A randomized double-blind placebo control trial conducted by Yang et al. investigated a commonly used TCM medication Xin-yi-san [XYS] compared to placebo in the treatment of

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Table 1 Traditional Chinese medicine

Study	Treatment	Control	Number	Findings
Lenon et al. [6]	RMIT Chinese medicine	Placebo	104	Equal safety, however, no benefit compared to placebo
Wang et al. [3]	Chinese herbal medicine	Placebo	533	Reduced total nasal symptom scores $P=0.003$ and a trend toward reducing total serum IgE levels $P=0.19$
Yang et al. [4]	Xin-yi-san (XYS)	Placebo	108	Decrease in nasal airflow resistance and increase in nostril dissection areas. IGE/XYS treatment resulted a 15–20 % reduction in both Der p1 ($P=0.007$) and Der p2 ($P=0.001$) whereas no difference was observed in the placebo group.
Acupuncture				
Cao et al. [7]	Acupuncture, cupping, medication	Medication	120	All groups showed improvement in symptom scores. Acupuncture + cupping + medications showed most improvement.
Wang et al. [8]	Acupuncture	Medication	81	Acupuncture provided greater symptom scores than loratadine azelastine combination [$P<0.05$].
Brinkhaus et al. [9••]	Acupuncture	Sham acupuncture	422	Statistically significant improvement in symptom scores compared to sham therapy and medication alone. However, these improvements were small.
Choi et al. [10•]	Acupuncture, sham acupuncture	No therapy	238	Total nasal symptom score was improved in both sham and active acupuncture compared to no therapy.
Xue et al. [11]	Acupuncture	Sham acupuncture	63	Acupuncture showed a benefit in regard to total symptom scores $P=0.04$ and sneezing score $P=0.01$.
Xue et al. [11]	Acupuncture	Sham acupuncture	30	Significant improvement in five-point symptom scores with acupuncture over sham therapy
Magnusson et al. [13]	Acupuncture	Sham acupuncture	40	Reduction in IgE specific levels to Mugwort $P=0.019$ and skin test reaction [$P=0.004$]; no difference in clinical symptoms
Brinkhaus et al. [14••]	Acupuncture, medication	Medication	5237	Additional prescribed medication due to allergic rhinitis was used significantly ($P=0.01$) less often by patients in the acupuncture group (59 %) compared with patients in the control group (68 %).
Fleckenstein et al. [12]	Acupuncture	Sham acupuncture	24	Statistically significant improvement in nasal sickness scores; secondary outcomes did not show a significant difference between both groups.
Homeopathy				
Goossens et al. [22]	Homeopathic mixture	Placebo	46	RQLQ was used for evaluation showing a baseline of 5.5 and after 4 weeks of treatment RQLQ of 1.6 [$P=0.0001$]
Aabel et al. [21]	Betula 30c [birch]	Placebo	66	No difference in symptoms from placebo
Friese et al. [23]	Unknown homeopathic remedy	Placebo	144	Homeopathic treatment group dropped from 12.1 to 5.9, placebo dropped from 11.7 to 11.0 [$P<0.001$].
Kim et al. [24]	S.W. desert mix	Placebo	40	Significant positive changes from baseline with a 4-week homeopathic preparation [$P<0.05$]
Taylor et al. [20]	30c Mixed dilution of allergens	Placebo	50	Improvement in nasal airflow mead difference 19.8 l/min [$P=0.0001$], visual analogue score showed a reduction of 28 % in homeopathic group vs 3 % reduction in placebo group [$P=0.0007$]
Weiser et al. [25]	Luffa Compositum Heel	Cromolyn sodium spray	146	No difference in RQLQ scores between groups

allergic rhinitis with efficacy measured by more objective means [4]. The study utilized objective and subjective

measurements of improvement that revealed a decrease in nasal airflow resistance and an increase in the nostril areas

with YYS as compared to placebo. There was an additional finding of suppression of serum IgE levels and IgE selective to dust mites as well as a reduction of selective IgE15-20 % compared to placebo in both Der p1 [$P=0.007$] and Der p2 [$P=0.001$] [4].

A TCM allergic rhinitis nasal formulation [ARND] was studied in a randomized double-blind placebo control study of 35 patients by Chui et al. ARND is composed of Herba Centipedae [small Centipeda] 23 %, Herba Menthae [peppermint] 16 %, Radix Paeoniae Alba [white peony root] 16 %, Radix Scutellariae [Baikal skullcap root] 10 %, Radix Glycyrrhizae [licorice root] 6 %, Radix Platycodi [Platycodon root] 6 %, Floz Lonicerae [honeysuckle flower] 5 %, Fructus Zizyphi Jujubae [Chinese date] 5 %, Rhizoma Coptidis [coptis root] 4 %, Radix Ledebouriellae [Ledebouriella root] 5 %, and Pericarpium Citri Reticulatae [tangerine peel] 4 % and was compared to placebo with primary outcomes based on clinical symptom scores and quality-of-life scores. The results demonstrated mild improvement overall with greatest improvement in quality of sleep [$P<0.05$], appetite, and overall joy [5]. Interestingly, similar other mint-containing herbal formulations have similar claims in which peppermint oil (e.g., Sinusol™, Hydrasense™, BioMint™) actually contains two primary components, menthone and menthol, which are inter-related. Menthone breaks down as oil matures during the flower development stage to form menthol and neomenthol. This is important because menthol contributes to peppermint oil's characteristic taste, aroma, cooling, and decongestant properties.

Lenon et al. designed a double-blinded randomized placebo control trial including 104 patients and utilizing a TCM formulation known as RMIT 102, a combination of *Astragalus membranaceus* [milk vetch root], *Bupleurum* Chinese D.C [thorowax], *Glycyrrhiza uralensis* [Chinese licorice], *Magnolia liliflora* [magnolia lily], *Mentha haplocalyx* Briq. [Japanese mint], *Saposhnikovia divaricata* [siler root], and *Scutellaria baicalensis* Georgi [Chinese skullcap]. There was no benefit or statistical improvement between the treatment and placebo groups during the 10-week course of this study. While no change in symptom scoring was noted, there was also no impact on liver or kidney function making this a safe treatment based on this small test population [6].

The evaluation of the studies is difficult to compare head to head due to the nature of these therapies containing multiple formulations and the low power of the studies (Table 1). The numerous combinations make it difficult to highlight the active ingredient that resulted in the reduction in IgE and symptom improvement. Overall, TCM has demonstrated mixed efficacy; however, further well-constructed placebo-controlled studies are needed. The establishment of the official Chinese Herbal Pharmacopie has greatly improved the standards and the overall safety of herbal components after there had been serious adverse events including fatalities with

contaminated components with aflatoxins and heavy metals such as lead.

Acupuncture

Acupuncture is one of the earliest therapeutic interventions of Chinese medicine with some sources describing the use of this therapy as early as 300 BC. Acupuncture is based on the manipulation of meridians or *qi*. *Qi* is the lifeblood of the body and is affected by the balancing of the five elements of TCM through placement of needles at key acupoints [2].

One randomized control trial performed by Cao et al. examined the utilization of acupuncture and medication vs acupuncture, cupping [a therapy utilizing heated glass to create local suction], and medication vs medication alone. The study demonstrated patient symptom score improvement with triple therapy when compared to acupuncture or cupping alone over a 6-month period. There is a strong potential for bias, as this was a non-blinded study [7] and patients received an oral antihistamine, loratadine, every other day for the first 30 days with results measured at the end of the 30 days and again at 6 months both demonstrating improvement with combined therapy [7].

In a randomized controlled trial by Wang et al., 81 patients were evaluated with the utilization of acupuncture compared to a combination of loratadine and azelastine. The patients reported improvement via symptom scoring demonstrating 95 % effectiveness in acupuncture group compared to 83 % in the medication group [$P<0.05$]. Nasal obstruction scoring and total symptom scores were also improved in the acupuncture group compared to the medication group. The study introduced a bias by providing patients with the combination of loratadine and azelastine for a 12-day period and then evaluating patients' symptom scores after 3 months to evaluate long-term benefit compared to acupuncture [8]. No treatment arm consisting of continuous therapy was included in this study.

A multicenter randomized controlled trial by Brinkhaus et al. evaluated 422 patients with acupuncture and cetirizine compared to sham therapy and cetirizine. The patients were evaluated before intervention and again at 7 weeks, 16 weeks with a final evaluation at week 60. The large study revealed an improvement in the acupuncture group vs sham [$P<0.001$]; however, these improvements were minimal and not clinically significant over the course of the year [9••].

In a randomized controlled trial evaluating real vs sham acupuncture compared to no therapy by Choi SM et al., 238 patients demonstrated that true acupuncture resulted in an improvement in total nasal symptom score compared to sham or no therapy [$P=0.03$]. These improvements were noted at 4 and 8 weeks of therapy. Interestingly, sham therapy was also

noted to be superior to no therapy; however, the improvement was less than that of true acupuncture [10•].

A similar study of 63 patients comparing sham vs true acupuncture utilizing the rhinoconjunctivitis quality of life questionnaire [RQLQ] demonstrated a benefit with regard to total symptom score [$P=0.04$] and most significantly in sneezing score [$P=0.01$] [11]. Another similarly structured study by Xue et al. supported these findings by demonstrating a reduction in nasal symptom scores compared to sham therapy [12]. In both studies, improvement was noted by week 4 of therapy with acupuncture vs sham three times per week [11, 12].

Magnusson et al. compared the efficacy of acupuncture vs sham therapy in a randomized controlled trial including 40 patients with a history of skin test-confirmed allergic rhinitis. The outcomes were measured at 12 months for the impact on symptom scores, visual analogue scales, reduction in skin test reactions, and levels of specific IgE levels. There was a reduction in sIgE in one allergen, Mugwort IgE [$P=0.019$], and skin test reaction [$P=0.004$]; however, other allergens did not demonstrate a similar trend, and given the low power of the study, there is a high potential for artifact as acknowledged by the author [13].

A large double randomized control trial was constructed by Brinkhaus et al. examining 5237 subjects evaluated by comparing acupuncture in addition to standard medical therapy vs standard medical therapy without acupuncture [14••]. During randomization, 487 patients were assigned to the acupuncture arm and 494 to the control arm. The remaining 4256 patients refused randomization and were also assigned to acupuncture group, thus introducing a potential bias. The study resulted in an improvement in the RQLQ score of 1.48 in the acupuncture with medical therapy group which was significant compared to medical therapy alone [$P<0.001$]. There was a statistically significant reduction in additional prescription of medication in the acupuncture group; 59 vs 68 % in the control group [$P=0.01$]. These improvements demonstrated more pronounced improvement by 3 months of intervention which continued out to 6 months [14••].

In a meta-analysis by Lee et al., seven well-constructed randomized controlled trials were evaluated, and it was shown that three of these studies failed to demonstrate superiority of acupuncture compared to placebo in the treatment of allergic rhinitis. Two of the studies demonstrated a favorable outcome for true acupuncture compared to sham acupuncture therapy with regard to improved nasal symptom scores over a 2-month period. In the final two studies, there was a statistically significant improvement in symptoms when acupuncture was added to traditional medical therapy [15].

Overall, there are mixed results regarding the efficacy of acupuncture in the treatment of allergic rhinitis. A large portion of the studies included small sample populations and were poorly constructed with significant difficulties regarding researcher and patient bias given the operators awareness of

real versus sham therapy when applying acupuncture. There is a clear need for further evaluation in regard to the potential efficacy of acupuncture in the treatment of allergic rhinitis.

In regard to the safety and cost-effectiveness of acupuncture therapy, several studies have been conducted. Acupuncture was deemed not to be a cost-effective addition to therapy in the USA; however, it was deemed a safe therapeutic intervention with a 671 events per 10,000 [16, 17]. In a safety analysis, 468 adverse events were recorded over a 3-year period. The most common adverse events included retained needles (31 %) and dizziness (30 %) with 95 % of all events deemed to be minor or not harmful [18]. While the evidence of the efficacy of acupuncture is not conclusive at this time, the low-risk safety profile of this therapy makes it a safe intervention in selected patients seeking alternative medical therapy.

Homeopathy

Homeopathy has been in practice since the nineteenth century, based upon the principle that disease can be attenuated by dilutions of substances that provoke these symptoms [19]. Homeopathy has been implemented in the treatment of allergic rhinitis in several studies (Table 1).

In a randomized controlled trial, Taylor et al. demonstrated a nasal airflow mean difference of 19.8 l/min [$P=0.0001$], visual analogue scores also showed a reduction of 28 % in the homeopathic group vs 3 % reduction in the placebo group over a 4-week period [$P=0.0007$]. There was an initial increase in rhinitis symptoms in the homeopathic group compared to placebo [$P=0.04$] at week 3 [20]. A larger study by Aabel et al. found no difference in symptom scores from placebo when evaluated weekly over a 4-week period [21].

A prospective open trial of 46 patients treated with homeopathic mixture resulted in a reduction in RQLQ from 5.5 at baseline to 1.6 after 4 weeks of therapy [$P=0.0001$] [22]. These findings were supported by the randomized controlled trial by Friese KH et al. of 144 subjects receiving homeopathic therapy vs placebo with outcomes revealing a decrease from 12.1 to 5.9 in sinus symptom scores compared to a decrease in placebo group from 11.7 to 11.0 [$P<0.001$] [23].

A study by Kim LS et al. in the USA utilized a dilution of south west desert pollen mixture for homeopathic therapy in 40 patients resulted in a reduction in symptoms based on RQLQ after 4 weeks of therapy [$P<0.05$] [24]. The duration of relief following intervention was unfortunately not investigated in this study.

In a double-blind equivalence study of 146 patients comparing cromolyn sodium spray to homeopathic mixture [Luffa Compositum Heel], there was no statistical difference between the two groups with outcomes measured by RQLQ [25].

It is estimated that 3–4 % of patients who utilize CAM use homeopathic therapy. While several meta-analyses on the efficacy of homeopathy have found no difference from

Table 2 Traditional Chinese medicine

Study	Treatment	Control	N	Findings
Schapowal et al. [27]	<i>Petasiters hybridus</i> [Butterbur]	Cetirizine	125	Equally effective based on SF-36 symptom score
Schapowal et al. [28]	<i>Petasiters hybridus</i> [Butterbur] high dose versus low dose	Placebo	186	Butterbur was superior to placebo [$P<0.001$] with high dose superior to low dose [$P=0.02$]
Schapowal et al. [29]	Butterbur or fexofenadine	Placebo	330	Both treatment groups were superior to placebo [$P<0.001$]; there was no difference between active treatment groups [$P=0.37$] evaluated by TNSS.
Lee et al. [30]	<i>Petasiters hybridus</i> [Butterbur] or fexofenadine	Placebo	16	Significant improvement in TNSS and PNIF compared to placebo, no difference between active treatment groups
Gray et al. [31]	<i>Petasiters hybridus</i> [Butterbur]	Placebo	35	No significant difference in TNSS and PNIF when compared to placebo
Saxena et al. [32]	Aller-7	Placebo	171	Significant decrease in nasal symptom score compared to placebo
Vyjayanthi et al. [33]	Aller-7	Placebo	48	Significant decrease in all nasal symptoms except for nasal stuffiness in greater than 75 % of patients

placebo, 75 % of patients utilizing homeopathy report subjective improvement [26].

Overall, evidence is mixed regarding the efficacy of homeopathy; however, these treatments have a low-risk safety profile. The combination of low risk, potential benefits, and high perceived value by patients makes homeopathy a CAM that has unclear benefits with little risk posed to the patient and its utilization should not be discouraged. Furthermore, well-constructed studies are needed to illicit the true potential benefits of homeopathic medicine.

Herbal Therapy

Herbal therapy is the combination of naturally occurring products utilized with the intention of reducing nasal symptoms. While much of the available literature on the use of herbal therapy is of poor quality, there are a few larger studies that have been identified as higher quality and are highlighted in Table 2. Two of the more well-studied and potential therapies include *Petasites hybridus* and Aller-7.

In a study by Schapowal et al., patients with allergic rhinitis were treated with either *P. hybridus* or cetirizine. The outcome revealed no significant intergroup differences [27]. A follow-up study of *P. hybridus* compared to placebo revealed the *P. hybridus* was superior to placebo in 186 patients with outcomes measured by total nasal symptom scores [28].

A third study was conducted by Schapowal et al. with comparison of *P. hybridus* to fexofenadine. This study revealed both treatments to be superior to placebo [$P=<0.001$] with no significant difference between active treatment groups [$P=0.37$] [29].

Lee et al. compared *P. hybridus* vs placebo in the treatment of 20 patients with allergic rhinitis. Participants evaluated by nasal peak flow following recovery from adenosine monophosphate nasal challenge demonstrated a 13 % improvement of nasal peak flow [30]. However, a study by Gray

et al. of 43 patients who were treated with *P. hybridus* vs placebo demonstrated no significant difference in nasal peak flows between the treatment group and control group at the conclusion of the study period [31].

Another promising product is Aller-7, a combination herbal medication, which was studied by Saxena et al. in 171 patients as compared to placebo. This study revealed a significant decrease in patient total nasal symptom score vs placebo [32]. Also, patients were noted to have an improvement in absolute eosinophil count, nasal peak flows, and mucociliary clearance time [31]. Likewise, another randomized double-blind trial evaluating Aller-7 by Vyjayanthi et al. compared Aller 7 vs placebo demonstrated a greater reduction in symptom severity scores with Aller 7 as compared to placebo [33].

These studies provide evidence of future potential benefit specifically in *P. hybridus* and Aller-7; however, further investigation is required given that three of the larger trials were funded by the manufacturer of *P. hybridus* extract. Confirmation through larger studies which evaluate both safety and efficacy are required to clearly define the role of herbal therapy in the treatment of allergic rhinitis [34••].

Conclusion

In the USA, CAM therapy is continuing to grow with 50 % of patients utilizing these treatments. A variety of therapies have demonstrated mixed results. Most studies utilized subjective symptom scores with some objective findings indicating potential benefit. Further investigation is required into the true benefits of these products. As there are minimal risks associated with the use of CAM therapies, the integration of these modalities into the standard of care will continue to require additional studies to assess their pharmacoeconomic value on

the improvement of the quality of life while maintaining a low adverse effect profile.

Compliance with Ethics Guidelines

Conflict of Interest John Kern and Leonard Bielroy declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the authors.

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