



Complementary and alternative medicine in pulmonology

John D. Mark^a and Youngran Chung^b

Purpose of review

To provide a comprehensive review of complementary and alternative medicine (CAM) therapies for the treatment of pulmonary disorders in children.

Recent findings

The use of complementary medicine (CAM) is commonly used by both children and adults with breathing problems, and especially in chronic pulmonary disorders such as asthma and cystic fibrosis. Many clinics and hospitals now offer CAM, even though most of the conventionally trained health practitioners have little knowledge or education regarding CAM therapies. Research in CAM that demonstrates overall benefit is lacking, especially in children. Often parents do not report CAM use to their child's healthcare provider and this could compromise their overall quality of care. Although many research studies evaluating CAM therapies have methodological flaws, data exist to support CAM therapies in treating children with pulmonary disorders.

Summary

This review examines the latest evidence of CAM use and effectiveness in children with pulmonary disorders. Physicians should be aware of the many CAM therapy options and the research surrounding them in order to provide their patients with the most current and accurate information available.

Keywords

asthma, complementary and alternative medicine, cystic fibrosis, integrative medicine

INTRODUCTION

Complementary and alternative medicine (CAM) is a term used when discussing healthcare approaches that are outside of mainstream or conventional medicine. The use of CAM therapies such as acupuncture, hypnotherapy, dietary supplements, aromatherapy, and homeopathy is common in both children and adults. The most recent National Health Interview Survey (NHIS) from the Centers of Disease Control and Prevention (CDC) estimated that 40% of adults and almost 10% of children had used CAM therapies in the previous year [1]. In children with chronic illness, this increases to more than 50%. CAM is now being used in many clinics and hospitals, even though most conventionally trained health practitioners have little knowledge or education regarding CAM and research in CAM establishing benefit has been lacking overall. What has also made the use of CAM challenging is that most patients or their parents do not report CAM use to their healthcare provider, and this could compromise the overall quality of care [2]. However, most pediatricians (83% in one study) would like

to learn more about CAM [3]. In children with pulmonary disorders, childhood asthma and cystic fibrosis are the two areas where CAM therapies have been primarily studied. Using these studies in children with asthma and cystic fibrosis, insight into other pulmonary disorders may be gained.

In a recent survey of over 5000 children with asthma, CAM use was 26.7% [4]. In this study, children with asthma who used CAM were compared to children who did not, and it was found that being female, having public insurance, reporting cost barriers to asthma care, having an asthma-related visit to an emergency room, and a history of

^aDepartment of Pulmonary Medicine, Lucile Packard Children's Hospital Stanford, Palo Alto, California and ^bDepartment of Pulmonary Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, USA

Correspondence to John D. Mark, MD, 770 Welch Rd, Ste 350, Palo Alto, CA 94304, USA. Tel: +1 650 723 8325; fax: +1 650 723 5201; e-mail: jmark@stanford.edu

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KEY POINTS

- CAM therapies are increasingly being used for children and adolescents with pulmonary disorders.
- A review of the literature found many small studies and descriptions of CAM therapies, but few randomized controlled trials, meta-analyses, or systematic reviews for the majority of therapies, especially in children.
- Although some CAM therapies are promising in such disorders as asthma and cystic fibrosis, the use of CAM therapies should only be considered with the guidance of a CAM-educated medical provider.
- The use of CAM therapies in children should be supported by the same high standards of scientific evidence as conventional treatments.

poorly controlled asthma showed a significant increase in CAM use. It was also found that 42% of uninsured children with asthma had used CAM in the previous 12 months compared to 24% of children insured privately. Breathing therapies, vitamins, herbal products, aromatherapy, and homeopathy were the most commonly used CAM therapies. Of note, 71% of CAM users reported use of one type of CAM therapy, 17% used two types, and 11% used three or more in the past 12 months for treatment of asthma. Although there was no decrease in adherence to controller medications in this survey with CAM use, this finding has varied in previous studies of both adults and children [5^a,6]. This variance may depend on the degree of asthma control, geographic location, and parental attitudes toward CAM [7]. One longitudinal analysis in pediatrics showed no effect of CAM use on future adherence to controller medication [8].

In a study of CAM use in 97 children and adults with cystic fibrosis (of which 81% of the respondents were parents of children), it was found that 75% of the patients used some form of CAM [9]. The majority (53%) used dietary supplements followed by mind–body medicine (MBM) (49%) and manipulative therapies (14.5%). This questionnaire study showed that 77% of the patients who used CAM felt it was useful, but only 53% of these families reported their use to their physicians. The high prevalence of CAM use may indicate the desire of parents and patients to have better control and self-management of their condition. In a recent study examining the parents of children with cystic fibrosis for using CAM, 24 parents were interviewed [10]. Prayer was the most commonly used CAM therapy (21 of 24 parents) in addition to spiritual modalities such as healing touch and meditation. Most parents (81%) felt that prayer was effective, but only two

of the parents reported that they had discussed the use of prayer with their child's pulmonologist.

DIETARY SUPPLEMENTS

The use of dietary supplements is prevalent in both children and adults with asthma [1]. Dietary supplements are products that are intended to supplement the diet and improve health. They include vitamins, minerals, and herbal medications, and may come in many forms such as pills, capsules, tablets, powders, or liquids (teas, decoctions, and tinctures). In most surveys, supplements are the most commonly used form of CAM for pulmonary problems [8]. However, dietary supplements, including herbal medications, do not have the same government oversight as conventional medications, and are treated more like food products [11]. In addition, many of these supplements have not been well described as to what their active ingredients are, and may have over a 1000 different ingredients. Many dietary supplements have a plant basis, so possible allergic reaction to components is a risk that needs to be considered, especially in children with asthma with multiple plant allergies.

Since there is no government manufacturing regulation, the quality and effectiveness of these supplements may depend on when they were harvested, where and how long they were stored, and what delivery form was used. These factors complicate research on dietary supplements, especially if compared to conventional therapies, since dietary supplements are often used in combination. Most studies that have been carried out are in cases of adults and children with asthma. A review of herbal preparation studies in asthma identified 26 trials of 20 different herbal preparations, and the majority of the studies reported no significant differences in measure of lung function or steroid dosage [12]. A few smaller studies reported improvement in forced expiratory volume in one second (FEV1) or airway hyper-responsiveness for herbal remedies such as Ding Chuan Tang [13], *Boswellia* [14], TJ-96-Saiboku-to [15], and *Tylophoraindica* [16]. A Cochrane review which reviewed 27 studies examining herbal interventions for chronic asthma in adults and children found that although use was prevalent, the wide variability of the compounds, poor study quality, and small sample size precluded endorsement of any specific herbal intervention for asthma [17].

There are some recent studies that have reviewed commonly used dietary supplements for pulmonary problems. Magnesium is found in the normal diet, but dietary surveillance studies have shown that children's mean intake of some minerals, including

magnesium, is below the recommended daily allowance (RDA) [18]. One study looked at the effect of oral magnesium on asthma control in adults with chronic asthma in a randomized placebo-controlled trial [19]. Oral magnesium was given for 6.5 months to 55 adults with mild to moderate asthma. Adults who received oral magnesium showed improvement in bronchial reactivity to methacholine and peak expiratory flow rate, and in subjective measures of asthma control and quality of life. In a randomized placebo-controlled study in children ($n=37$) aged 7–19 years, 2 months of oral magnesium supplementation reduced airway reactivity and skin responses to known allergens, as well as fewer asthma exacerbations needing rescue medications [20]. Another supplement that has been proposed to treat asthma is Pycnogenol. It has been used in adults and children with chronic inflammation-type disorders including asthma. Pycnogenol is a herbal dietary supplement derived from the French maritime pine bark and is standardized to 70% procyanidin. A small study in children with asthma in 2004 showed benefit [21]. However, the 2012 Cochrane review [22] analyzed 15 trials including two asthma studies ($n=86$) and found there was insufficient data to support Pycnogenol use for the treatment of any chronic disorder including asthma.

Omega-3-fatty acids been commonly promoted for pulmonary disorders such as asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis. In one double-blind crossover trial of 6 weeks' duration, a study of 23 adults with asthma showed that there was no change in bronchial hyper-responsiveness (BHR) (using inhaled mannitol), and no decrease in sputum eosinophils or inhibition of urinary excretion of mast cell mediators. The authors concluded that omega-3-fatty acids were not useful in the short-term treatment of mild to moderate asthma [23^{***}]. However, a Cochrane review [24] analyzed four studies ($n=91$) to evaluate whether supplementation with omega-3-fatty acids would decrease the morbidity and mortality in patients with cystic fibrosis, and if there were any identified adverse events associated with its use. The authors concluded that the regular use of omega-3-fatty acids may provide some benefit for patients with cystic fibrosis with rare adverse reaction. The benefits included improvement in lung function, Shwachman scores, and decrease in sputum volume (short-term study). There was also a significant increase in serum phospholipid essential fatty acid content and a drop in omega-6 fatty acid-to-omega-3 fatty acid ratio. In a longer-term study of 17 cystic fibrosis patients, there was a significant increase in the essential fatty acid content in neutrophil membranes and decrease in the leukotriene

B4-to-leukotriene B5 ratio compared to the placebo group [25].

Traditional Chinese medicine (TCM) uses herbal combinations that are individualized on the basis of a patient's specific symptoms. There have been several double-blind, placebo-controlled studies investigating both the safety and efficacy of herbs used in TCM [26]. In a recent study [27], 75 children were randomly divided into a Chinese medication group and a Western medication control group. The Chinese medication control group were given established Chinese herbal formulas. The Western medication group received a leukotriene receptor antagonist and a bronchial relaxant. The mRNA expression levels of interleukin (IL)-4, cysteinyl leukotriene receptor 1, and interferon (INF)-gamma in the peripheral blood were measured in both the groups. The Chinese medication group showed decreased levels of IL-4 and significant increase in INF-gamma levels. The authors concluded that the Chinese medication had a regulatory effect on the leukotriene receptor gene expression and the imbalance of Th1/Th2 immune cells. Another study using TCM investigated the effects of quality of life using a government-sponsored project questionnaire and how it was affected by TCM treatment in children over a 1-year period [28^{*}]. Fifteen hospitals and seven medical centers were included, and the children were placed in three groups: children treated with non-TCM; children treated with single TCM; and children treated with integrative TCM (conventional and herbs). The patients in the TCM groups exhibited greater therapeutic effects, did not require emergency department (ED) visits, or hospitalization. The children who received the combination TCM did better than the single TCM or the conventionally treated group.

Antioxidants (including vitamin A, C, and E) have been thought to be beneficial in many respiratory disorders such as asthma due to increased oxidative stress, which is an imbalance between reactive oxygen species and antioxidants and may result from increased exposure to air pollutants and decreased intake of certain fruits and vegetables. Reduced levels of vitamin E and C have been reported in the bronchoalveolar lavage in patients with asthma [29]. Meta-analysis of epidemiologic studies suggests low dietary intake of antioxidants, and higher asthma and allergy prevalence. A few small clinical studies suggest that specific antioxidants from diet or vitamin supplements may improve asthma control or lung function in children and adults with asthma. An excellent recent review of this area of interest concluded that the potential benefits and risks of trials of vitamin supplementation should be considered in special

situations for vulnerable populations who have deficiencies in dietary antioxidants and high exposure to environmental sources of oxidants [30¹¹]. A large prospective study of over 65 000 women from Shanghai examined baseline levels of urinary F2-isoprostanes, plasma concentrations of antioxidant micronutrients along with antioxidant enzyme activity. It was noted that lower measures of antioxidants were risk factors in the 150 women who went on to develop asthma. Supplementation may be a strategy for primary asthma prevention [31¹¹]. Another vitamin that has been studied in respiratory disorders in children is vitamin D. Studies have shown that supplementing with vitamin D may help prevent asthma exacerbations in children [32¹¹]. Other studies investigating early supplementation during pregnancy have not found a consistent association of low vitamin D levels and subsequent wheezing or allergies [33].

Probiotics have been studied in both asthma and cystic fibrosis. In children at risk for asthma, it has been hypothesized that this may be in part due to an unfavorable gut microbiota [34]. By modifying the microbiota with the supplementation of probiotics, this may reduce sensitization and inflammation, therefore preventing such things as eczema and asthma. Several prospective studies have been carried out, and supplementation with probiotics may help in preventing eczema, but not asthma in children [35,36]. The use of probiotics has also been studied to determine if their use may decrease the rate of respiratory exacerbations in cystic fibrosis. In a recent study, 61 patients with cystic fibrosis with mild to moderate lung disease were randomized in a double-blind, placebo-controlled manner and given *Lactobacillus reuteri* or placebo for 6 months. Pulmonary exacerbations were significantly reduced in the group receiving the probiotic compared to the placebo group as were upper respiratory tract infections. There were no significant differences in number or duration of hospitalizations for pulmonary exacerbations and gastrointestinal infections. The authors concluded that supplementation with *L. reuteri* may have a beneficial effect on the disease course in patients with mild to moderate cystic fibrosis lung disease [37¹¹].

ACUPUNCTURE

The WHO has endorsed acupuncture for asthma, whooping cough, insomnia, small airway obstruction, and allergic rhinitis [38]. The US National Institutes of Health consensus statement in 1997 had also endorsed acupuncture as an effective adjunctive treatment option for asthma [39]. A more

complete summary of acupuncture and pulmonary diseases can be found in a review article [40].

In the past few decades, systematic reviews on acupuncture have been inconclusive due to variability in study outcomes. This is thought to be due to methodological problems (e.g. difficulty in blinding, inability to standardize acupuncture points, and lack of true sham points). The most recent systematic review of laser acupuncture for asthmatic children from several clinical trials also showed contradictory results due to small sample sizes, variation in type of patients, interventions, and outcome measures. The authors concluded that there is no compelling evidence to say that laser acupuncture is ineffective, but that further rigorous studies were needed [41]. Since that review, one study concluded that low-intensity laser acupuncture was a well-tolerated and effective treatment for asthmatic children. In this study, 50 asthmatic children randomly selected from a clinic were evaluated 1 month after receiving 10 laser acupuncture sessions. Statistically significant improvement ($P < 0.001$) was seen in nocturnal symptoms, exercise tolerance, FEV1, and FVC, as well as asthma control questionnaire, and the majority of the patients became well controlled on decreased inhaled steroids and short-acting β 2-agonist [42]. A longer follow-up study would be of interest to determine the length of treatment needed to sustain these results.

In recent years, there has been research on the biological effects of acupuncture. In a study of acupuncture administered three times per week for 5 weeks in patients with allergic asthma, there was a statistically significant decrease in the secretory and total IgA in their saliva and nasal secretions, as well as their total serum IgE, IL-2R, and T lymphocytes and eosinophils [43].

HOMEOPATHY

Homeopathy is based on the concept that a substance which produces a particular constellation of symptoms when given in a pharmacologic/toxic dose can treat a patient who presents with similar symptoms when the substance is given in ultradiluted form. Physiologic effects induced by such ultramolecular dilutions have been demonstrated at the cellular level such as the inhibition of human basophil degranulation by a homeopathic dilution of histamine [44]. To date, the field of homeopathy has lacked an explanation for its mechanism. The hypotheses for the mechanism of action are naturally thought to be biophysical rather than pharmacological because the substance is diluted beyond Avogadro's number [45–48]. A recent study showed

a statistically significant alteration of gene expression by a homeopathic dilution of *Gelsemium sempervirens* – a medicinal plant employed as an anxiolytic [49]. More follow-up studies such as this would help improve the understanding of homeopathy.

There were 288 randomized controlled trials (RCTs) of homeopathy published as of 2013, of which 45% were positive, 45% inconclusive, and less than 10% negative [50]. One study which was a prospective randomized double-blind, placebo-controlled study in adults showing homeopathic potassium dichromate decreased tenacious tracheal secretions and resulted in earlier extubation in intubated COPD patients compared to controls [51]. A more recent prospective, observational, longitudinal study of individualized homeopathic medicines used adjunctively in 30 children with asthma showed statistically significant improvement in severity, frequency of nocturnal asthma attacks or awakenings, use of inhalers and oral corticosteroids, as well as pulmonary function test parameters at 3 and 6 months [52]. A review article on homeopathic research in the treatment of respiratory allergies and asthma reviewed evidence from controlled trials that were deemed to be of high quality. The authors concluded that homeopathy may offer possible options to conventional treatment of respiratory allergies and asthma [53].

There was a cost–benefit evaluation study of homeopathic versus conventional therapy in 105 consecutive patients with chronic respiratory conditions (asthma, allergic rhinoconjunctivitis, recurrent upper respiratory infection and otitis media, chronic bronchitis). A review of medication records compared the impact of drug costs of those attending a homeopathic versus a conventional clinic. After 1 year, a 71% reduction in medication cost was seen in the homeopathic treatment group versus the group that was treated only with conventional drugs [54]. There is a need for future high-quality research in homeopathy, and challenges remain due to the individualized selection of homeopathic remedies.

MIND–BODY MEDICINE

Mind–body medicine encompasses techniques such as clinical hypnosis, biofeedback, relaxation techniques, meditation, breathing exercises, as well as yoga, tai chi, and qi gong, which involve some body work. It is well documented that stress can enhance airway inflammation in asthma by modulating immune cell function through neural and hormonal pathways [55–57]. Many MBM techniques, including hypnosis, can decrease stress and anxiety

and potentially modulate these pathways. Since its emergence in the late 1950s, efficacy has been demonstrated for a wide spectrum of conditions including asthma [58]. Several case series on the use of hypnosis for problems seen in a pulmonary clinic have been reported [59,60]. These included pain control, making medication taste more palatable, and functional disorders such as anxiety, chest pain, dyspnea, habit cough, hyperventilation, sighing, vocal cord dysfunction, as well as persistent asthma.

A review of hypnosis for asthma concluded that hypnosis likely helps with the behavioral/emotional component of asthma and has a potential to decrease severity and relieve airway hyper-responsiveness, although evidence was insufficient for decreasing airway inflammation [61]. In a recent 2014 review of hypnosis for asthma, cystic fibrosis, dyspnea, habit cough, and vocal cord dysfunction, hypnosis had a positive effect, but the authors acknowledged the weakness of these studies as the majority of the literature was comprised of case series and retrospective studies, with only a single small randomized study [62[■]].

Other techniques such as guided imagery and relaxation techniques have also been shown to benefit asthma, with increase in FEV1 predicted [63] and also reducing the level of IgE in dust mite allergic adults [64]. Although yoga is frequently used by patients with asthma, prior systematic reviews did not support its efficacy for asthma [65–67]. Since then, another systematic review and meta-analysis of yoga based on 14 RCTs showed evidence of the positive effects of yoga on patient-reported outcomes and pulmonary function compared with usual care and psychological interventions, but not compared with breathing interventions or sham yoga interventions. This study concluded that yoga could be considered an ancillary intervention or an alternative to breathing exercises for asthma [68].

LIFESTYLE

There has also been some evidence that once a child has developed a respiratory condition such as asthma, certain lifestyle changes such as improved sleep quality and structured exercise may improve lung function and quality of life. In a study of over 500 children of whom 263 had asthma, it was found that snoring was more prevalent in children with asthma as was sleep-disordered breathing (SDB) on the basis of the Pediatric Sleep Questionnaire (PSQ). This study also showed that the prevalence of SDB increased with increasing severity [69[■]]. Addressing sleep problems would be an important step in asthma control in children. Exercise may also contribute to improve asthma symptoms (if well

controlled), as well as improving airway hyper-reactivity. In a systematic review and meta-analysis to determine the effect of exercise training on quality of life (QoL), BHR, lung function, and exercise capacity were completed. A total of 17 studies ($n=599$) were reviewed and exercise training showed a significant improvement in days without asthma symptoms, FEV1, QoL, and exercise capacity. The authors concluded that physical activity should be recommended as a supplementary therapy to medication [70].

CONCLUSION

Complementary and alternative medicine therapies are frequently being utilized by children and adults with respiratory disorders. These CAM therapies are being used with conventional therapies by many practitioners, as well as hospitals and clinics. However, research evaluating the effectiveness of CAM is difficult due to the individualized nature of most therapies and methodological problems. Even deciding which type of CAM therapies should be considered is not clear. An increasing interest in nutrition, and special diets (Mediterranean diet) was not discussed in this review, but has been recently reviewed in detail [71]. There has been increasing research in CAM therapies, but overall research is still lacking in most areas, especially in children with pulmonary disease. It is important that healthcare providers, especially pediatricians, should become more familiar with CAM therapies so they may be able to advise, assist, and educate patients and families in making decisions as to what CAM therapies to consider. Practitioners should also know how to monitor the effectiveness of the various CAM therapies used by their patients and monitor for any side effects or untoward outcomes.

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Conflicts of interest

There are no conflicts of interest.

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- of outstanding interest

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