

Complementary and alternative medicine for the treatment and diagnosis of asthma and allergic diseases

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ABSTRACT: *Complementary and alternative medicine for the treatment and diagnosis of asthma and allergic diseases. G. Passalacqua, E. Compalati, M. Schiappoli, G. Senna.*

The use of Complementary/Alternative Medicines (CAM) is largely diffused and constantly increasing, especially in the field of allergic diseases and asthma. Homeopathy, acupuncture and phytotherapy are the most frequently utilised treatments, whereas complementary diagnostic techniques are mainly used in the field of food allergy-intolerance.

Looking at the literature, the majority of clinical trials with CAMS are of low methodological quality, thus difficult to interpret. There are very few studies performed in a rigorously controlled fashion, and those studies provid-

ed inconclusive results. In asthma, none of the CAM have thus far been proved more effective than placebo or equally effective as standard treatments. Some herbal products, containing active principles, have displayed some clinical effect, but the herbal remedies are usually not standardised and not quantified, thus carry the risk of toxic effects or interactions.

None of the alternative diagnostic techniques (electrodermal testing, kinesiology, leukocytotoxic test, iridology, hair analysis) have been proved able to distinguish between healthy and allergic subjects or to diagnose sensitizations. Therefore these tests must not be used, since they can lead to delayed or incorrect diagnosis and therapy. *Monaldi Arch Chest Dis 2005; 63: 1, 47-54.*

Keywords: *Complementary/alternative medicines, asthma, allergic diseases, diagnosis, therapy.*

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Introduction

Medical approaches to diseases which differ from the conventional allopathic medicine are generally grouped, in western countries under the umbrella of *alternative medicines*. Indeed, some of these techniques represent the traditional medicine in several other countries and are part of the traditional medicine. Thus, the term *complementary/alternative medicine (CAM)* should be preferred, since it does not imply an aprioristic negative judgment. Apart from those medical systems with a millenary history (Chinese, Japanese, Ayurvedic), there are numerous more recent CAM techniques (for instance homeopathy), where the number is constantly increasing. In particular, in the last decades, several holistic/behavioural approaches have been introduced. A list of the CAMs is reported in table 1.

CAMS are widely and preferentially used to treat chronic diseases, such as headache, musculoskeletal pain, irritable bowel, urticaria. Allergy and allergic diseases (including asthma and rhinitis) are therefore important fields for CAM, where homeopathy, acupuncture, herbal medicines and yoga are the most utilised techniques [1]. Also in the field of food allergy/intolerance, there is a wide and increasing use of diagnostic techniques

that are often associated with behavioural/holistic or dietary treatments.

According to the most recent data, the percentage of subjects using or who have used CAMS in the general population ranges between 25 and 30%, up to 50% in Australia [2, 3] and USA [4]. Moreover, these percentages are constantly increasing, particularly in the last 20 years [5]. Recent studies have reported figures as high as 70% in Germany and France [6]. This widespread use is of course related to an impressive economic business [7, 8]. Similar data has been reported also in the pediatric age, where at least 50% of children resulted to have been treated with CAMs [9]. In Italy, only two epidemiologic studies are available [10, 11], showing that among allergic patients about 30% are using CAMs. Interestingly, it emerged that about 80% of specialists were favorable to CAM and judged them of benefit for patients. The reasons for using CAMs usually reported by patients are: distrust in conventional medicine, the belief that CAMs are more natural and safe, and the need for a more strict relationship with the physician

As a matter of fact, allergists and pulmonologists have more and more often to afford the problem of patients who want to try CAMs in substitution of traditional medicine, or who have received

Table 1. - Complementary/alternative medicines

| Acupuncture | SYSTEMATIC MEDICINES | OTHER |
|----------------------------|-------------------------------|----------------------------|
| Homeopathy | Traditionale chinese medicine | Aromatherapy |
| Herbal medicine | Japanese (Kampo) | Bach's flowers |
| | Indian (Ayurveda) | Chromotherapy |
| PHYSICAL TECHNIQUES | Sciamanic medicine | Enematherapy (hydro-colon) |
| Chiropractic | | Hypnosis |
| Massage | BEHAVIORAL | Hopi candles |
| Spinal manipulation | Dissociated diets | Iridology |
| Breathing control | Anthroposophy | Reflexology |
| Yoga | Clinical ecology | Speleotherapy |
| | Biofeedback | Urine-therapy |

a particular diagnosis for their allergy based on CAM diagnostic techniques. Thus, it is important that physicians are aware of the efficacy and contraindications of CAMs in order to provide patients with experimentally-supported information.

In this regard, due to the large diffusion of CAM, the high prevalence of allergic diseases, and the not negligible costs, that proof of efficacy are incontrovertible is definitely needed [12]. Only randomized controlled (possibly placebo-controlled) trials can be considered when judging the efficacy of a CAM treatment. Looking at the literature, the vast majority of the clinical trials with CAMs have a low qualitative level [13], thus making the results often difficult to interpret. On the other hand, it is claimed that "holistic" approaches cannot be standardised and submitted to rigorous study designs, because the standardisation itself introduces a confounding factor [14]. Finally, it has to be considered that some of the CAM techniques are self-applied (Yoga, relaxation techniques, biofeedback) and therefore cannot be blinded.

Acupuncture

Acupuncture is a cornerstone of the Traditional Chinese Medicine, and is widely used for chronic illness, including asthma. Acupuncture is intended to restore the balance of "vital flows" by inserting needles at exact points of the body surface, where the "meridians" of the flows lay. Specific points can be stimulated also by pressure or laser application. There are numerous studies of acupuncture in asthma, whereas few data is available for rhinitis and other respiratory diseases. An early systematic review of acupuncture in asthma was conducted by Kleijnen in 1991 [15]. In that review, 13 controlled studies were considered (6 double blind and 7 single blind): four of the double blind studies were negative and six of the single blind ones were positive. Based on the methodological quality of the studies, the Authors concluded, more than 10 years ago, that beneficial effects of acupuncture were more likely to be found in the low-quality studies. Things have not changed after 15 years: the most recent Cochrane

reviews [16, 17], included 11 studies with 324 participants: trial reporting was poor, and quality was judged inadequate. Indeed, looking only at those studies performed with a rigorous methodology (i.e. randomised, controlled and blinded) [18-26], the effects of acupuncture are not different from the placebo treatments. Of note, only in two studies [21, 26] transient and mild benefits were demonstrated. Thus, the conclusion derived from meta analysis studied and clinical trials is that acupuncture is not effective to treat asthma.

Almost all studies of acupuncture in allergic rhinitis are not randomised, not controlled, or use weak methodologies [27-29]. There is only one randomised crossover trial [30] in seasonal rhinitis, with low methodological quality. In this study active acupuncture significantly reduced the symptom scores, without any change in the need for rescue medications. To date, based on the small amount of experimental data, acupuncture cannot be considered as a viable alternative to standard treatments for rhinitis.

Surprisingly, there is little data on the use of acupuncture in COPD, despite the fact that it is a typically chronic illness. One open study [31] demonstrated that both acupuncture and acupressure improve the quality of life of patients with COPD. In another recent randomised controlled study [32], it was shown that both real and sham acupuncture improved the dyspnea of COPD patients, without difference between active and control treatment. So far there is no experimentally supported indication to the use of acupuncture in COPD.

Homeopathy

Homeopathy is based on the belief that symptoms of a disease can be cured by the same substance that provokes them, if given at ultra-dilution. Homeopathic remedies are therefore chosen according to symptoms, not to disease, and prepared with a special manual technique called "potentiation". Homeopathy is a holistic approach to medicine that pays a special attention to the homeopath-patient relationship, and involves also behavioral and dietary approaches. Homeopathy has

Table 2. - Randomized controlled studies with acupuncture in asthma

| AUTHOR | DESIGN | N. PATS | DUR AT | Main Results |
|-------------|-----------------|---------|--------|--|
| Biernacki | crossover | 23 | 1 day | Improved QoL and ↓ use of bronchodilators with both sham and real intervention |
| Christensen | Parallel group. | 18 | 5 wk | ↓ symptoms and use of bronchodilators in the active group |
| Gruber | Crossover | 44 | 1 day | No effect on isocapnic hyperventilation |
| Joos | Parallel group | 36 | 4 wk | No difference in pulmonary function and self-assessment. ↓ use of bronchodilators in both groups |
| Malmstrom | Parallel group | 24 | 15 wk | No effect on isocapnic hyperventilation with both treatments |
| Medici | Parallel group | 64 | 16 wk | No clinical difference among real, sham and placebo. Transient ↓ in PEF variability. ↓ blood eosinophils in real VS sham |
| Shapira | Crossover | 23 | 3 wk | No effect on PEF, FEV ₁ , use of beta2 agonists and methacholine challenge |
| Tandon | Crossover | 15 | 5 wk | No difference in PEF, FEV ₁ , use of beta2 agonists and asthma score between groups |
| Tashkin | Crossover | 25 | 4 wk | No difference in FEV ₁ , use of beta2 agonists and asthma score between groups |

↓ = decrease; ↑ = increase.

been extensively studied in allergic diseases, and there are numerous well conducted and rigorous trials in both asthma and rhinitis. There are three randomized, placebo controlled, double blind studies in asthma [33-35]: these studies failed to demonstrate a mesurable clinical benefit on symptoms and functional parameters in adults [33, 34], and children [35].

There are also some studies in rhinitis [36-40]. The controlled study using a homeopathic dilution of *Galphimia glauca* for pollinosis, found no significant difference between active and placebo treatment [36]. Reilly *et al*, performed an early DBPC study in seasonal allergic rhinitis, evaluating a visual analog-scale and the intake of chlorpheniramine, and found a significant difference in favour of homeopathy for both parameters [37]. Another DBPC trial compared cromolyn and an intranasal homeopathic remedy (*Huffa comp. Heel*) and found no difference between the two treatments, both effective, in seasonal allergic rhinitis [38]. Taylor *et al* [59] performed another DBPC study in 50 patients with perennial allergic rhinitis. This study showed a significant improvement only in nasal flow in the active group, whereas the clinical improvement on a visual analog scale was the same in both active and placebo group. A homeopathic dilution of birch pollen provided only a marginal effect in seasonal allergic rhinitis [40], or even aggravated the symptoms during the pollen season [41]. In summary, there are three positive and three negative studies of homeopathy in rhinitis, therefore it cannot be recommended as an alternative to standard treatment. Finally, the recent reviews including all the trials

(independent of the disease and the methods), conclude that some effect of homeopathy exists, but positive results are usually obtained in low-quality trials [17, 42-44].

No randomized and controlled study of homeopathy in chronic obstructive pulmonary disease, chronic Urticaria or food allergy is available in literature.

Phytotherapy

The traditional allopathic medicine is largely based on substances derived from plants and herbs (e.g. theophylline, salicylates, digitalis, morphine). Also the Chinese, Japanese and Ayurvedic medicines largely use herbs, often in fixed mixtures (e.g. *ma huang* and *saiboku-to*). The literature on herbal remedies is impressive, due to the large variety of herbs and their combinations used: *tylophora indica*, *boswellia serrata*, *pychrorryza kurroa*, *koleus forskholii*, *gynko biloba*, *urtica* and others. All these studies are generally of low quality (for a review see 45), but in many cases, a clinical effect can be measured in several diseases, including rhinitis and asthma. This is not surprising, because most of the herbs utilised contain pharmacologically active ingredients. Positive results were obtained in rhinitis and asthma with the mixtures of herbs used in the traditional Chinese medicine, which contain ephedrine and atropine. For instance, some studies with *Tylophora indica* [46, 47] have reported positive results in asthma. One double blind placebo controlled study performed in asthma subjects showed that the gum resin of

Table 3. - Studies with homeopathy

| Author | DIS * | TREATM | CONTROL | N PATS | FINDINGS |
|------------|-------|--------------------------------------|-------------------------------|--------|--|
| Aabel | R | Birch 30c | Placebo | 66 | No effect on symptoms |
| Aabel | R | Birch 30c | Placebo | 73 | No effect on symptoms |
| Lewith | A | Dust mite homeopath | Placebo | 186 | No difference between active and placebo in FEV ₁ , PEFr, symptoms, use of b2 agonists and asthma score |
| Reilly | A | 30c dilution of allergens | Placebo | 21-18 | No change in PEFr, pulmonary function and histamine challenge. Significant improvement in the VAS |
| Reilly | R | 30c dilution grass pollen | Placebo | 155 | ↓ symptom score, VAS and use of antihistamines |
| Taylor | R | 30c dilution of allergens | Placebo | 50 | ↑PNFR morning and evening. No difference betw groups in VAS and symptom score |
| Weiser | R | Nasal <i>Luffa comp</i> | Nasal cromone | 135 | Homeopathy = nasal cromone, both effective on symptoms |
| White | A | Individ. homeopathy + drugs | Placebo + drugs | 74 | No difference between active and placebo in Asthma QoL, PEFr, use of beta2 agonists, missing days |
| Wiesenauer | R | <i>Galphimia</i> homeopathy dilution | Conventional dilution/placebo | 104 | No significant difference between active and placebo treatments |

* R = Rhinitis, A = Asthma; ↓ = decrease; ↑ = increase.

Boswellia serrata (used in Ayurvedic remedies) was able to significantly improve symptoms and FEV₁ after a 6-week course [48]. Two studies reported that *saiboku-to* (TJ96) improved asthma symptoms, exerted a steroid-sparing effect, reduced bronchial responsiveness and decreased sputum eosinophils in asthma patients [49, 50]. One controlled study in 8 asthmatics showed that an extract from Ginko biloba protected against bronchial specific challenge [51]. Despite the positive results reported, the quality of these studies was in general low and therefore not useful for giving recommendations. In fact the most recent meta analysis of herbal therapy in asthma produced negative results [52].

The same as for asthma happens with rhinitis, where some randomised controlled trials provided positive results. For instance, one study with a mixture of 18 Chinese herbs showed a significant efficacy of the treatment in seasonal rhinitis (symptoms and QoL) [53], and another the Chinese herb formulation *biminne* was statistically effective in perennial rhinitis [54]. One recent study using a combination of acupuncture and Chinese herbs found a significant effect on symptom scores and quality of life in seasonal allergic rhinitis [55]. On the other hand, a rigorous double blind randomized controlled trial showed that grapeseed extract was not more effective than placebo for ragweed induced rhinitis [56]. The most recent trial focused on butterbur (*Petasites hybridus*) extract in rhinitis. The first one [57] compared butterbur 400 mg daily and cetirizine 10 mg and found that

both treatments were equally effective on symptom scores and QoL. The second study [58], in perennial rhinitis, confirmed that butterbur 400 mg was equivalent to fexofenadine 120 mg in controlling symptoms.

As far as COPD is concerned there is a controlled study utilizing the ginseng root (100 mg b.i.d.), where the herb, as add-on to standard therapy improved the tolerance to exercise [59].

Herbal remedies contain pharmacologically active substances that are responsible for the clinical effects. At the same time, the active ingredients may also induce undesirable side effects [60, 61]. Moreover, compared with proprietary marketing drugs, herbal remedies carry the risk of adulteration, incorrect collection of plants, wrong preparation and inappropriate/incorrect dosing [62].

Behavioural, physical and other complementary treatments

Physical techniques (e.g. breathing control, Yoga techniques and chiropractic/spinal manipulation) have been proposed in patients with chronic respiratory illness with the aim of improving the respiratory pattern. Indeed, most of the rigorous trials of chiropractic/spinal manipulation in asthma [63-65] failed to demonstrate a clinically relevant effect. In other studies, the effects were marginal [66-68]. The literature reviews conclude that breathing and yoga techniques can have some effect on self-perceived well being, but they cannot be rec-

ommended as an effective treatment for asthma [69, 70]. Also behavioural techniques such as biofeedback and hypnosis have been sometimes applied in asthma, generally in low quality studies, but the overview of the literature concluded for no effect [71-72].

Also for behavioural/physical techniques, the literature concerning COPD is surprisingly poor. There is a randomised controlled open trial with relaxing techniques providing encouraging results concerning the perception of dyspnea in COPD patients [73]. There are also two studies with music-therapy [74, 75] and one with Yoga techniques [76] in COPD, but none of those studies were randomized or controlled. No controlled/randomized clinical trial in rhinitis or asthma has been performed with other alternative medicines (aromatherapy, chromotherapy, Bach's flowers, anthroposophy, clinical ecology). Therefore these techniques must not be recommended.

Complementary/alternative diagnostic procedures

There are numerous complementary/alternative diagnostic techniques available (table 4), often not based on experimental proof of concept [77]. These alternative techniques are largely used in the field of "food allergy/intolerance". This is probably due to the fact that many clinical diseases (e.g urticaria, migraine, irritable bowel, chronic fatigue syndrome, hyperkinetic syndrome) are often considered as "allergic", despite no formal demonstration is provided. In other words, "food allergy" is often considered as a simple pathogenic explanation of those symptoms which cannot be clearly classified. Indeed, the alternative techniques are also sometimes used to diagnose respiratory allergy. When evaluating the validity of such tests, a comparison with the "gold standard" (that is double blind placebo controlled food challenge for food allergy or skin prick test for respiratory allergy) should be performed.

Electrodermal tests are based on the hypothesis that skin electrical conductance changes when the subject comes into contact (even indirect) with noxious, allergenic or toxic substances. The skin conductance is measured through proper devices at specific acupoints, while the substances to test are introduced in the circuit. The earliest studies, not randomised and not blinded, reported a good cor-

relation between electrodermal tests and specific IgE to inhalant allergens [78] and intradermal test [79] respectively. Indeed, the most recent studies, performed in double blind and randomized fashion, failed to demonstrate any correlation between the results of electrodermal testing and ascertained sensitizations [80, 81]. In synthesis, the electrodermal test could not identify the allergic subjects and, in addition, displayed an unacceptable variability.

Leukocytotoxic tests are based on the hypothesis that peripheral leukocytes modify their shape or volume when they come into contact with noxious or allergenic substances [82]. The few studies available have shown an intrinsic and unacceptable variability of the method and a complete absence of correlation with clinical parameters [83-85].

Kinesiology. This method is based on the assumption that a reduction of the muscular strength of contraction occurs when the subject comes into contact with a noxious or allergenic substance. Usually, the subject has to keep in his/her hands or touch (but the direct contact is not mandatory) a vial containing the substance to test. The changes in muscle contraction are evaluated directly by the examiner or with a dynamometer. There are few well established studies evaluating the kinesiologic test [86, 87], invariably failing to demonstrate the diagnostic value and reproducibility of the procedure.

Provocation/neutralization. This procedure is both a diagnostic and therapeutic tool. It is based on the belief that intradermal (or even sublingual) administration of noxious or toxic substances provokes "untoward effects" within 10-12 minutes. The test is considered positive irrespective of the type of effect observed or reported. Thus, the test is not standardized and is largely dependant on the personal interpretation. After a positive identification, the same substance that provoked the symptom(s) is given again to "neutralize" the adverse effect. Apart from numerous case reports and uncontrolled trials, there are few reliable studies on this test. Jewett and colleagues (88) in a double blind procedure found that active substance provoked symptoms in 16% and placebo in 24%, without correlation with clinical history. Fox *et al.*, (89) in another controlled trial in 132 patients concluded that "the results of provocation-neutralization testing, using symptoms alone as an indicator of neutralisation, should not be

Table 4. - Alternative diagnostic procedures

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|---|
| ELECTRODERMAL TESTS (Electroacupuncture): VEGA (TM), Dermatron (TM), DBE (TM) |
| BIOCHEMICAL TESTS: Leucocytotoxic test, ALCAT (TM), hair analysis |
| KINESIOLOGY: DRIA test and similar |
| IRIDOLOGY |
| PROVOCATION / NEUTRALIZATION: sublingual and intradermal |

used as a basis for clinical intervention". A near-fatal event was even reported in a subject suffering from mastocytosis [90].

Other tests. It has been claimed that it is possible to diagnose allergies/intolerances by analysing the hair content of metals and micronutrients. There is one controlled trial showing that the results of the test are completely random and that the variability among different operators and laboratories approximates 100% [91]. Iridology was proven to be completely unreliable and not supported by scientific evaluations as well [92].

In conclusion, none of the alternative/complementary techniques for diagnosing allergy/intolerance (especially in the field of food allergy) is supported by a solid scientific basis. They must not be used in clinical practice [77, 93, 94].

Conclusions

Available scientific evidence does not support a role for CAMs in general in the treatment of asthma and other allergic diseases. More specifically, none of the proposed CAMs has been demonstrated capable of replacing the existing standard therapy. Moreover, the majority of the published studies have significant methodological flaws (e.g. small number of patients, lack of proper controls, inadequate blinding) that weaken the conclusions. Subjects treated are often not properly characterized in regard to asthma severity and use of conventional drugs. More rigorous studies are needed to confirm or to disprove the efficacy of CAMs. Some favourable results have been indeed obtained with phytotherapy, and this is not surprising since many herbs contain pharmacologically active principles. The main problem with herbal remedies is that they are usually non standardized, and represented by variable mixtures of substances. This fact may result in toxicity, drug interaction and adulteration. Therefore, further investigation into herbal treatments is important because it may possibly lead to the development of new useful medications.

Physicians often find CAM intimidating, because they are unaware of the clinical evidence and feel uncomfortable advising their patients on its efficacy. So there is definitely a need for improved education and knowledge among physicians, because the majority of patients are using or have used some form of CAMs. Physicians should inquire and discuss this issue in order to promote more successful treatment to their patients.

From a diagnostic point of view, to date there is no complementary or alternative diagnostic procedure which can be recommended as a meaningful element in the work-up of allergic diseases. This is especially true for food allergy for which properly performed oral double-blind placebo controlled food challenge still represents the gold standard diagnostic procedure. Ineffective diagnostic procedures may be costly for the consumer and result in delayed therapy or incorrect diagnosis.

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