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Review

Efficacy, effectiveness and cost-effectiveness of acupuncture for allergic rhinitis — An overview about previous and ongoing studies

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ABSTRACT

In general, allergic rhinitis can be divided into seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). In the following sections a summary of efficacy and effectiveness studies is presented. For this narrative review we selected studies based on the following parameters: publication in English, sample size ≥ 30 patients, and at least 6 acupuncture sessions.

Most studies aimed to evaluate the specific effects of acupuncture treatment. Only one study evaluated effectiveness and cost-effectiveness of additional acupuncture treatment. The studies which compared acupuncture with sham acupuncture always used a penetrating sham control. A medication control group was used in only two studies and one study combined acupuncture and Chinese herbal medicine.

This overview shows that the trials on efficacy and on effectiveness of acupuncture are very heterogeneous. Although penetrating sham controls were used predominantly, these also varied from superficial penetration at acupuncture points to superficial insertion at non-acupuncture points. Although there is some evidence that acupuncture as additional treatment is beneficial and relatively cost-effective, there is insufficient evidence for an acupuncture specific effect in SAR. In contrast, there is some evidence that acupuncture might have specific effects in patients with PAR. However, all of the published efficacy studies are small and conclusions should be made with care. Further studies with a larger sample size are urgently needed to draw more rigorous conclusions and the results of the ongoing trials will provide us with further information within the next two years.

Contents

1. Introduction

Allergic rhinitis (AR) has become a major health problem with a marked increase in the prevalence of AR in the past two decades (Van

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Cauwenberge et al., 2000). Direct costs from AR in Europe are estimated to be 1.0–1.5 billion Euro annually, whereas indirect costs are estimated at 1.0–2.0 billion Euro (Van Cauwenberge et al., 2000). Despite advances in conventional therapy, a remarkable number of patients with AR are turning to complementary medicine for relief (Krouse and Krouse, 1999; Schäfer et al., 2002). The lifetime prevalence of CAM use in patients with AR ranges from 27% to 46%, and many of the patients who have not yet used CAM, intend to do so in the future (Krouse and Krouse, 1999; Schäfer et al., 2002). The prevalence of acupuncture, a form of CAM, in AR patients is estimated to be between 17% and 19% (Krouse and Krouse, 1999; Schäfer et al., 2002).

The authors of two recently published systematic reviews drew the conclusion that there is currently insufficient evidence to support or refute the use of acupuncture in patients with AR (Roberts et al., 2008; Lee et al., 2009). Seven relevant RCTs were included in the systematic review by Roberts et al. A meta-analysis of the data failed to show any lasting benefits of acupuncture treatment for symptom severity scores, or serum IgE measures in AR, which could not have been accounted for purely by chance (Roberts et al., 2008). In the review by Lee et al., seven high quality trials were included. All RCTs tested the efficacy of acupuncture by assessing symptom relief of AR. Three RCTs failed to show superiority of acupuncture for treating or preventing symptoms for seasonal AR compared with sham acupuncture (Lee et al, 2009). For perennial AR, one study reported favourable effects of acupuncture on rhinitis symptoms and another trial found positive results for nasal symptoms compared with sham acupuncture. Two RCTs, which compared acupuncture with conventional oral medication, positively favoured acupuncture.

The authors of both systematic reviews pointed out that previous studies on the efficacy of acupuncture in AR have suffered from a variety of methodological limitations, such as small patient numbers or the lack of a sham acupuncture control group. Overall, there is currently insufficient evidence to support or refute the use of acupuncture in patients with AR and therefore, a large well conducted RCT, which overcomes the identified methodological problems is required (Roberts et al., 2008).

Clinical research in complementary medicine can focus on different questions regarding the efficacy of a treatment compared to placebo in an experimental setting, or the effectiveness of an additional treatment in a real world setting (Witt, 2009). Both efficacy and effectiveness studies are available for acupuncture, however, the main focus was on efficacy. 'Efficacy' refers to 'the extent to which a specific intervention is beneficial under ideal conditions', whereas 'effectiveness' is a 'measure of the extent to which a specific intervention works when deployed in the field of usual care' (Garber and Tunis, 2009). Cost-effectiveness research aims to evaluate 'efficiency'. Efficiency is a measure of the relation between resource inputs (costs) and health outcomes and providing evidence on whether healthcare resources are being used to get the best value for money.

Allergic rhinitis can be divided into seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). In the following sections a summary of efficacy and effectiveness studies is presented. For this narrative review we selected studies based on the following parameters: publication in English, sample size ≥ 30 patients, and at least 6 acupuncture sessions.

2. Results

2.1. Data available on efficacy, effectiveness and cost-effectiveness

Most studies attempted to evaluate the specific effects of the acupuncture treatment. Only one study evaluated effectiveness and cost-effectiveness of additional acupuncture treatment. The studies which compared acupuncture with sham acupuncture always used a penetrating sham control and a medication control group was used in only two studies. One study combined acupuncture and Chinese herbal medicine. The studies are summarized in Table 1.

2.2. Efficacy of acupuncture for seasonal allergic rhinitis (SAR)

To date, there is no clear evidence for the acupuncture treatment of SAR. From the three trials presented here comparing acupuncture with sham acupuncture, one study detected a significant difference and two did not. In addition, there is one large ongoing three-armed multicenter RCT comparing the efficacy of acupuncture with sham acupuncture and standard treatment. One further trial evaluated a combination of acupuncture and Chinese herbal medicine and found a difference compared to the control group. All completed studies were relatively small with the largest sample size being 102 patients.

2.2.1. Acupuncture vs sham acupuncture

In the study by Williamson et al. (1996) 102 patients received either acupuncture (3 or 4 times weekly for 10 weeks) or sham acupuncture with minimal insertion and no manipulation at non-acupuncture points. The main outcome criteria were a symptom score (Likert scale, 10 points) and the use of medication. After 10 weeks there were no significant differences between the groups for the symptom score and the use of medication.

Magnusson et al. (2004) found that acupuncture was not superior to sham acupuncture in reducing clinical symptoms. This study compared acupuncture with sham acupuncture (1 to 2 cm lateral to the related points) in 40 consecutive patients with SAR and a positive skin test. Patients were assessed prior to treatment and after twelve months. No differences in clinical symptoms were seen between acupuncture and sham acupuncture.

In contrast to the other studies, Xue et al. published a randomized controlled crossover trial which showed a significant difference between acupuncture and sham acupuncture (Xue et al., 2002; Xue et al., 2007). 30 participants were randomly assigned to two groups and treated with acupuncture or sham acupuncture three times per week for four consecutive weeks, followed by a crossover of treatments for a further 4 weeks. Acupuncture treatment was provided following syndrome differentiation according to Chinese Medicine. For sham acupuncture, the needle was inserted only 1.5 cm lateral to the related points. Outcome measures included subjective symptom scores using a five-point scale, relief medication scores and adverse effect records, which were assessed before, during and after the treatments. Twenty-

Table 1
Summary of the presented RCTs. (Selection criteria: ≥30 patients, ≥ 6 acupuncture sessions; publication in English).

Research question/ trials	Patient	Comparison			Result
		Acu. vs. sham	Acu. vs. routine care	Acu vs. standard	
Efficacy SAR					
Williamson et al., 1996	102	x			−
Xue et al., 2002	30	x			+
Magnusson et al., 2004	40	x			−
Plus herbal medicine					
Brinkhaus et al., 2004	52	x			+
Efficacy PAR					
Ng et al., 2004	72	x			+
Li et al., 2007	100			x	+
Xue et al., 2007	80	x			+
Effectiveness					
*Brinkhaus et al., 2008	981		x		+
Plus costs					
*Witt 2009	981		x		

+ = acupuncture superior compared to control group; − = acupuncture not superior compared to control group; * data based on the same clinical trial.

six participants completed the study. There was a significant difference in the five-point scale for nasal and non-nasal symptoms between the two groups in favour for acupuncture. No significant differences were shown for the medication scores.

2.2.2. Acupuncture and herbal medicine

In another RCT including 52 patients, who were given a combination of acupuncture and Chinese herbal medicine (Brinkhaus et al., 2004), the authors concluded that this combination might be an efficacious treatment for SAR. In this study all patients received acupuncture treatment once per week and the respective Chinese herbal formula as a decoction three times daily for a total of 6 weeks. Compared to patients in the control group, patients in the group showed a significant improvement after treatment regarding SAR symptoms and for the Rhinitis Quality of Life Questionnaire. However, no differences between the two groups were reported for the Allergic Rhinitis Symptom Questionnaire.

2.3. Efficacy of acupuncture for perennial allergic rhinitis (PAR)

The evidence for the efficacy of treatment of PAR seems to be better than for SAR. Two trials compared acupuncture with sham acupuncture, one of them in children. The third trial compared electro-acupuncture with a medication control. In addition, there is a large ongoing trial currently being performed in two countries (Korea and China).

2.3.1. Acupuncture vs. sham acupuncture

There is only one study on children (Ng et al., 2004), where 72 children were randomized to receive acupuncture or sham acupuncture (acupuncture points, superficial needling 0.3 cm). Both the assessing pediatricians and the patients were blinded. There were significantly lower daily rhinitis scores and more symptom-free days in the acupuncture group, during both the treatment and the follow-up periods. The visual analog scale scores for immediate improvement after acupuncture also favoured the acupuncture group. However, there were no significant differences in the daily relief medication scores, blood eosinophil counts, serum IgE levels, or nasal eosinophil counts (except for the IgE levels).

In the trial by Xue et al. (2007), 80 adult patients were randomly assigned to receive acupuncture or sham acupuncture. For sham acupuncture, the needles were inserted 1–1.5 cm from acupuncture points (shorter needles and a superficial needling technique were applied). After a one week baseline period, participants were treated for 8 weeks and were followed for another 12 weeks. After 8 weeks of treatment, the weekly mean difference from the total nasal symptom score from baseline was significantly better than with sham acupuncture. The individual symptom score decreased significantly with acupuncture for rhinorrhoea but not for the other symptoms. At the end of the follow-up period, the more pronounced difference from baseline for total nasal symptoms and all four individual symptom scores, was still apparent.

2.3.2. Electro-acupuncture

Li et al. (2007) compared the clinical effects and neuroimmunological mechanism of electro-acupuncture and medication in 100 patients. In one group, patients received electro-acupuncture (5–10 mA, 80–100 Hz, and 30 min of stimulation) with a semi-standardized intervention design (daily for 10 days). Patients in the medication group were treated with Cetirizine (10 mg/times, t. i.d, per os). Before and after the treatment, blood samples were collected for plasma vasoactive intestinal peptide and substance P. After the treatment, the effect on the electro-acupuncture group was significantly higher compared to medication. The plasma level vasoactive intestinal peptide was markedly lower in the electro-acupuncture group than in the medication group, while no significant difference was found for substance P levels.

2.4. Effectiveness and cost-effectiveness research

The aim of a large acupuncture study from Germany was to assess the effectiveness and cost-effectiveness of additional acupuncture treatment in patients with allergic rhinitis (Brinkhaus et al., 2008; Witt et al., 2009). This study is part of the Acupuncture in Routine Care (ARC) project, a large research initiative on acupuncture initiated and funded by the German statutory health insurance companies (Cummings, 2009). The design of this trial takes the pragmatic approach (Zwarenstein et al., 2008), as this approach was used for the first time to evaluate acupuncture for allergic rhinitis, we will present the methodology and results in greater detail.

The Acupuncture in Routine Care Study was a study in which patients who agreed to randomization (central telephone randomization with random list generated with SAS) were included in a multicenter randomized controlled trial with a non-randomized cohort. They were allocated either to an acupuncture group or to a control group. The patients in the acupuncture group received immediate acupuncture treatment whereas those in the control group received delayed acupuncture treatment after three months. Patients who declined to be randomized were included in a third arm and also received immediate acupuncture treatment (non-randomized acupuncture group). The study period per patient was six months: a three month treatment phase followed by a three month follow-up period. The protocol of this study was approved by the local ethics review boards.

Each patient in both the randomized and non-randomized acupuncture groups received up to 15 acupuncture sessions during the first three months and no acupuncture during the subsequent three month follow-up period. The control group was not allowed to use any kind of acupuncture during the first three months, but received acupuncture between months three and six of the study. In all three treatment groups, the patients were allowed to use any additional conventional therapy. For the study, each patient could be treated individually and the number of needles and the acupuncture points used, were chosen at the physicians' discretion. The primary outcome measure was to evaluate the effectiveness of acupuncture in SAR, using the Rhinitis Quality of Life Questionnaire (RQLQ) score, three months after treatment initiation. The secondary outcome was general quality of life measured with the SF-36. Costs considered were from direct health care, such as the cost of acupuncture, physicians' visits, hospital stays (private expenses were not included) as well as prescription medication (including patient's co-payment). The cost perspective of the study was societal. We calculated 1) the overall costs during the study period of three months after randomization, including costs not related to AR and 2) diagnosis-specific costs using ICD-10 codes to identify costs due only to AR and related conditions. For statistical and economic analyses please see (Brinkhaus et al., 2008; Witt et al., 2009).

Of 5237 patients (mean [SD] age, 40 [12] years; 62% women), 487 were randomly assigned to acupuncture and 494 to the control group, 4256 were included in the non-randomized acupuncture group. Cost data was available for 825 (84%) of all randomized patients (418 acupuncture; 407 control). These patients were included in the cost-effectiveness analysis. Patients in the acupuncture groups received a mean of 9.9 ± 3.0 (mean $\pm$ SD) acupuncture sessions (randomized acupuncture, 10.3 ± 2.6; non-randomized acupuncture, 9.9 ± 3.0).

The primary effectiveness analysis from the RQLQ at three months showed an improvement in disease specific quality of life by 1.48 ± 0.06 (mean $\pm$ SE) in the acupuncture group and by 0.50 ± 0.06 in the control group (three-month scores were 1.44 ± 0.06 and 2.42 ± 0.06, respectively; difference, 0.98 ± 0.08; $P<0.01$). At three months, improvement was similar in the non-randomized acupuncture group compared to the randomized acupuncture group 1.71 ± 0.02 to 1.51 ± 0.02 and 1.71 ± 0.05 to 1.51 ± 0.05; difference 0.006; 95% confidence interval, 0.107 to 0.118; $P = 0.92$).

For the 981 patients who were included in the cost-effectiveness analysis, the quality of life measures with the SF-36 after three months

was higher in the acupuncture group than in the control group (Physical Component Score 51.99 ± 0.33 (adjusted mean ± SE) vs. 48.25 ± 0.33, P<0.001 and Mental Component Score 48.55 ± 0.42 vs. 45.35 ± 0.42, P<0.001). This resulted in QALY 0.026 ± 0.0048. The overall costs were higher in the acupuncture group than in the control group (acupuncture group 763 €, 95% confidence interval: 683, 844 compared with the control group 332 €, 95% confidence interval: 252, 412). The incremental cost-effectiveness ratio was €17,377 per quality-adjusted life year, but more favourable for women (€10,155) than men, (€44,871) and was robust in sensitivity analyses.

2.5. Perspectives

Results of two large trials will be available within the next two years. One ongoing study on the efficacy of acupuncture for SAR, is currently being performed by our Institute (Brinkhaus et al., 2010). The aim is to investigate whether acupuncture is non-inferior or superior to (a) sham acupuncture and (b) rescue medication in the treatment of SAR. In total, 422 patients with clinical symptoms and positively tested to both birch and grass pollen, will be randomized in a 2:1:1 ratio to one of three groups: (a) semi-standardized acupuncture plus rescue medication (Cetirizin); (b) sham acupuncture at non-acupuncture points plus rescue medication; or (c) rescue medication alone for 8 weeks (standard treatment group). Acupuncture and sham acupuncture will consist of 12 treatments per patient over 8 weeks. The main outcome measures will be the overall mean scores of the Rhinitis Quality of Life Questionnaire and the Rescue Medication Score between weeks 6 and 8 in the first year adjusted for baseline values.

Another ongoing study that evaluates the efficacy of acupuncture for PAR is currently performed in China and Korea (Kim et al., 2009). 238 patients will receive either acupuncture or sham acupuncture (both three times per week for a total of 12 sessions over 4 weeks) or no treatment (waiting-list group). The primary outcome between the groups is a change in the self-reported total nasal symptom score from baseline at the fourth week. Secondary outcome measures include the Rhinitis Quality of Life Questionnaire and a total non-nasal symptom score.

3. Conclusion

This overview which is no systematic review shows that the trials on acupuncture on AR are very heterogeneous. Although penetrating sham controls were mainly used, these also varied from superficial penetration at acupuncture points to superficial insertion at non-acupuncture points. Although there is some evidence that acupuncture as an additional treatment is beneficial and relatively cost-effective there is insufficient evidence for an acupuncture specific effect in SAR. In contrast there is some evidence, to date, that acupuncture might have positive specific effects in patients with PAR. However, all of the published efficacy studies are small and conclusions should be made with care. Further studies with larger populations are urgently needed to draw more rigorous conclusions and the results of two large ongoing trials will provide us with further information within the next two years.

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