Protocol

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Review question(s)

What are the efficacy and safety of Modified Yupingfeng Formula for the

treatment of Allergic Rhinitis in children?

Searches

We will search the following electronic databases from inception until May

2015: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL),
EMBASE. The following Chinese electronic databases will be searched: China
Network Knowledge Infrastructure (CNKI), Chinese Biomedicine (CBM),
Chinese Scientific Journals Database (VIP) and Wan Fang Database.
Unpublished postgraduate theses in Chinese databases will also be searched.
We will screen the reference list of the retrieved articles for potentially eligible
studies.
No language restriction will be applied.

The specific search terms of PubMed were as follows:
#1 Search (((((((anaphylactic rhinitis [Title/Abstract]) OR allergic rhinitis
>Title/Abstract]) OR nasal allergy [Title/Abstract]) OR perennial allergic rhinitis
>Title/Abstract]) OR rhinallergosis [Title/Abstract]) OR hay fever[Title/Abstract])
OR pollinosis [Title/Abstract]) OR seasonal allergic rhinitis [Title/Abstract])
#2 Search ((Yupingfeng [Title/Abstract]) OR Chinese herbal medicine
[Title/Abstract]) OR Chinese medicine [Title/Abstract])
#3 Search (((children [Title/Abstract]) OR child [Title/Abstract]) OR kids
Search terms of other databases can be obtained from the author on request.

**Types of study to be included**

We will include randomized clinical trials to assess the beneficial effects and safety of Modified Yupingfeng Formula for the treatment of Allergic Rhinitis in children.

**Condition or domain being studied**

Allergic rhinitis, which can be divided into seasonal or perennial, is a common nasal allergy in children. The typical symptoms are including frequent sneezing, an itchy and runny nose, nasal congestion, itchy and watery eyes, and an impaired sense of smell. The prevalence of allergic rhinitis may vary within and among countries due to the presence of different allergens. In developed countries, the incidence of allergic rhinitis is up to 40%, and in China, the incidence is between 3.3% and 43.0% in different area. Allergic rhinitis has a significant negative impact on children’s quality of life, mood, memory and other medical conditions such as allergic cough, allergic conjunctivitis and asthma.

Current treatments of modern medicine include avoiding contact with allergen, antihistamine drug, intranasal corticosteroids, nasal decongestant, mast cell stabilizer, anticholinergic drug, specific immunotherapy and surgery.

Modern medicine and Chinese medicine are agree that the fundamental cause of allergic rhinitis is allergic constitution, and all kinds of allergen are inducing factors. Though they are in accord on pathogenesis, the treatments are different. The Modern medicine emphasized avoiding allergen, but some kinds of allergen can’t be avoided absolutely. The specific immunotherapy was considered the only treatment against etiology,
but with high incidence of adverse reactions and long-term therapy. Unlike modern medicine, Chinese medicine puts more emphasis on improvement of allergic constitution and doesn’t require the patients to avoiding allergen. Chinese medicine has many ways to improve allergic constitution with fewer side effects, such as Chinese herbal medicine, acupuncture, moxibustion, and acupoint application.

Yupingfeng Formula is the common traditional Chinese medicine which can improve allergic constitution, and widely be applied for children’s allergic rhinitis. Yupingfeng Formula was a famous formula developed by an ancient famous doctor Danxi Zhu of Yuan Dynasty. Yupingfeng Formula consists of three herbs: Astragalus membranaceus, Rhizoma Atractylodis Macrocephalae, Radix Ledebouriellae Divaricatae.

Many clinical trials are reported that Yupingfeng Formula has dual-directional regulation effects on human’s immune system. On the one hand, it could effectively improve the patient’s Th1 / Th2 immune imbalance, inhibiting generation of IgE to inhibit Type I allergy. On the other hand, it could increases the amount of IgG, the peripheral blood levels of CD3+, CD4+ and CD4+ / CD8+ to enhance the immune function of the body.

The TCM doctors usually treat the allergic rhinitis of children by Chinese traditional medicine prescription consists of Yupingfeng Formula and other herbs which can relieve nasal symptoms, such as Fructus xanthii, Lily magnolia, Asarum, peppermint, Acorus tatarinowii Schott.

Although a lot of reports of clinical trials on Modified Yupingfeng Formula for the treatment of Allergic Rhinitis of children in China are available, few systematic analyses and syntheses are identified. This systematic review aims to assess the effectiveness and safety of Modified Yupingfeng Formula for the treatment of Allergic Rhinitis, in order to provide evidence for clinical practice in Otolaryngology or allergic disease of Chinese medicine.

**Participants/ population**
Inclusion: children (age<18 years old) with allergic rhinitis regardless of the disease severity. Because the nasal structure of children are different from the adults', and the difference of physical structures will affect the clinical efficacy.

**Intervention(s), exposure(s)**

Modified Yupingfeng Formula in any preparations such as pills, capsules, decoctions, and tablets, orally taken, for the treatment of allergic rhinitis in children were included. The treatment duration was no less than 14 days. Modified Yupingfeng Formula prescribed by practitioners according to TCM syndrome differentiation. The prescription must include the three original herbs of Yupingfeng Formula, beyond that, may add other Chinese herbs.

**Comparator(s)/ control**

The controls could be no intervention, placebo, medication. Trials testing combination of Modified Yupingfeng Formula and medication compared with the same medication were also included.

**Context**

The study setting could be out-patient or inpatient, but hospital based. Exclusion criteria are: Multiply published trials, poor data authenticity studies (suspected fraud or plagiarism and could not get the information from confirmation by contacting the author), or trials with missing data not available from contacting the authors.

**Outcome(s)**

**Primary outcomes**

- Improvement of symptoms including nasal symptoms (nasal congestion, rhinorrhoea, sneezing, itchy nose) and non-nasal symptoms (itchy eyes, watery eyes and itchy ears), using symptom scores or scales.

**Secondary outcomes**

- Quality of life.
- Serum IgE level
• Recurrence rate
• Adverse events

Data extraction, (selection and coding)

Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources will be screened independently by two review authors (NN Chen and X Liang) to identify studies that potentially meet the inclusion criteria outlined above. The full text of these potentially eligible studies will be retrieved and independently assessed for eligibility by two reviewers. Any disagreement will be resolved through discussion with a third reviewer (HM Zhang).

A predesigned form will be used to extract data from the included studies for assessment of study quality and data analysis by two individual authors, and any discrepancies will be identified and resolved through discussion with a third author where necessary. Extracted information will include: study population, age and baseline characteristics; details of the intervention and control conditions; follow up time and outcome measures.

Risk of bias (quality) assessment

Two review authors will independently assess the risk of bias using Cochrane tool of Risk of bias. The following items will be assessed:
• Random sequence generation (selection bias)
• Allocation concealment (selection bias)
• Blinding (performance bias and detection bias)
• Incomplete outcome data (attrition bias)
• Selective outcome reporting (reporting bias)
• Other bias.

For each included study we will give a description supporting our judgment for each item. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
**Strategy for data synthesis**

We will summarize data using risk ratios (RR) with 95% confidence intervals (CI) for binary outcomes or mean difference (MD) with 95% CI for continuous outcomes. If different measurement scales are used, standardized mean difference (SMD) analyses will be performed. For cross-over trials, only the first intervention will be included. If required data are not reported, we will request data from corresponding author. We will use fixed effects model unless there are evidence of heterogeneity.

Heterogeneity will be assessed using both the Chi-squared test and the I-squared statistic. We will consider an I-squared value greater than 50% to be indicative of substantial heterogeneity. We will conduct sensitivity analyses based on study quality, if necessary. Funnel plots will be generated to detecting publication bias if more than ten trials are identified.

We will tabulate the findings by a Summary of finding table.

**Analysis of subgroups or subsets**

If the necessary data are available, subgroup analyses will be done for different outcome measures.

**Dissemination plans**

We will submit our findings to a high impact journal to publicize the findings internationally.

**Competing interests**

The authors declare that they have no competing interests.