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Review

Herbal medicines for treating acute otitis media: A systematic review of randomised controlled trials

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ABSTRACT

Introduction: This systematic review aimed to assess the clinical evidence for the widespread use of herbal medicines in treating acute otitis media.

Methods: Eleven electronic databases, including MEDLINE, EMBASE, and the CENTRAL were searched, without language limitations. All randomised controlled trials involving the use of herbal medicines, alone or in combination with conventional therapies, for acute otitis media were included.

Results: We identified 4956 studies, of which seven randomised clinical trials met the inclusion criteria. The overall risk of bias of the included trials was relatively high or unclear. Treatment with Longdan-xiegan decoction or Shenling-baizhu powder, combined with antibiotics, appeared to be more effective than treatment with antibiotics alone in terms of the proportion of patients with total symptom recovery. Moreover, combination treatment of Sinupret® and antibiotics facilitated the recovery of middle ear conditions and hearing acuity.

Conclusions: Despite some indications of potential symptom improvement, the evidence regarding the effectiveness and efficacy of herbal medicine for acute otitis media is inconclusive due to the poor quality of trials included. Moreover, we only analysed seven trials in this review. Therefore, to properly evaluate the effectiveness of herbal medicine for acute otitis media, systematic reviews based on more rigorously designed randomized trials are warranted in the future.

1. Introduction

Acute otitis media (AOM) is one of the most frequently diagnosed infections in infants and children, with more than 80% of children experiencing AOM at least once, and it is the most common cause for physician visits and consultation.[1,2] The worldwide incidence of AOM is 10.85%, and 21 thousand people die globally each year due to complications of otitis media.[3] Furthermore, the socioeconomic burdens of AOM are considerable; the AOM outpatient health care cost is $314 per child each year, and the total expenditure per year for otitis media is estimated to be in excess of $5 billion in the United States (US).[4,5]

For most children, antibiotics is not warranted because antibiotics have no immediate effect on pain in children with AOM, and only a slight effect on pain in the days following administration in several studies[6]. In addition, a greater percentage of children who receive antibiotics experience side effects, such as vomiting, diarrhoea, and rash, than those who receive a placebo.[6] Moreover, antibiotic use has the drawback of increasing the prevalence of resistant bacterial pathogen.[7,8] Furthermore, decongestants, antihistamines, and steroids are not beneficial in the treatment of AOM.[9,10]

In recent years, a large number of population with recurrent disease have chosen complementary and alternative medicine (CAM) and the total expenditure per year for the remedy of CAM is estimated $22 million in US.[11] A study showed that 42% of the population in US used CAM, with 12% of the population using herbal medicine (HM) in 1997.[12] In addition, a 2007 report by the National Center for Complementary and Alternative Medicine showed that 17.7% of population used herbs.[13] The extensive use of CAM, including herbal medicine, is apparent in otitis media[14]; one study showed that 46% of children with recurrent episodes of AOM have had experienced with some component

Abbreviations: AOM, acute otitis media; HM, herbal medicine; RCT, randomised controlled trial; RR, risk ratio; MD, mean difference; CI, confidence interval; LDXG, Longdan-xiegan; SLBZ, Shenling-baizhu; TM, tympanic membrane

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of CAM.[15–17] However, in spite of increased use in otitis media, evaluating of the efficacy of CAM medication is rarely performed due to certain difficulties, such as unclear time to effect and low economic incentive of research.[17]

Some studies have revealed that herbal extract ear drops may be more beneficial for reducing the pain of AOM than anaesthetic ear drops,[18] and an oral herbal medicine, Juzen-taiho-to, has been shown to reduce the frequency of AOM, the duration of fever, and the need for administration of antibiotics, as well as significantly reduce the number of total and emergency hospital visits.[19] Therefore, given its immunity-boosting and nutrition-improving effects, Juzen-taiho-to is recommended for treating recurrent AOM in the Japan Subcommittee of Clinical Practice Guidelines.[20]

However, to our knowledge, there has been no comprehensive evaluation of clinical studies on the beneficial and adverse effects of HM on AOM. Here, we provide the first systematic review of the evidence related to the use of HM for the treatment of AOM.

2. Methods

2.1. Protocol registration

This systematic review was registered in an international prospective register of systematic reviews under the registration number PROSPERO: CRD42013004836 (available URL:http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013004836).

2.2. Data sources

The following five databases were searched, from their inception to July 2016: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials [CENTRAL], the Cumulative Index to Nursing and Allied Health Literature [CINAHL], and the Allied and Complementary Medicine Database [AMED]. We also searched one Chinese database (China Network Knowledge Infrastructure [CNKI]) and five Korean databases (Oriental Medicine Advanced Searching Integrated System [OASIS], DataBase Periodical Information Academic [DBPIA], KoreaMed, Research Information Sharing Service [RISS], and the Korean Studies Information Service System [KISS]). The details of the MEDLINE search strategy are presented in the Appendix A. Additionally, the reference lists of all relevant articles were searched manually for additional trials. Hard copies of all retrieved articles were read in full.

2.3. Study selection and extraction

Two authors (MJS and YHK) independently reviewed the titles and abstracts, and extracted the data using a predefined data-extraction form. The following information was obtained from the included trials: the first author and year of publication, the country of origin of the paper, type of disease, mean age, duration of disease, sample size, experimental intervention, control group, outcome measure, and adverse effects. The following criteria were used to identify studies for inclusion in the review:

● Type of study

Randomised controlled trials (RCTs) or quasi-RCTs that reported the effects of HM on AOM were included.

● Type of participant

Studies that evaluated patients with a diagnosis of AOM were included. We excluded studies of patients in whom ventilation tubes had been placed, those with an anatomical deformity, or those with chronic immunocompromised states.

● Type of intervention

We included trials that evaluated orally administered HM alone or a combined therapy involving HM and a conventional therapy (antibiotic drugs, decongestants, antihistamines, or topical analgesia, but not surgery), versus the same conventional therapy alone. Therapy with HM included the use of a single herb, an individually prescribed herbal formula, and herbal products extracted from natural herbs. We included all types of herbal formulations.

● Type of comparison

Both active control and placebo were acceptable.

● Types of outcome measures

Trials reported at least one of the following primary and secondary outcome measures: the proportion of patients with pain or the intensity of pain, or the proportion of patients with fever or the intensity of fever. Secondary outcome measures extracted were as follows: abnormal tympanometry findings at various time-points (4–6 weeks and 3 months) as a surrogate measure for hearing problems caused by middle-ear fluid, tympanic membrane (TM) perforation, contralateral otitis (in unilateral cases), AOM recurrences, serious complications related to AOM, adverse effects likely to be related to HM, quality of life, and duration of remission.

2.4. Risk of bias assessment

The risk of bias was assessed in seven domains: random sequence generation, allocation concealment, assessor blinding, blinding of participants, incomplete outcome data, selective reporting, and other biases according to the domain-based evaluation.[21] Judgement for the risk of bias in seven domains was assessed using criteria for judging risk of bias in the “Risk of bias” assessment tool of Cochrane handbook.[21] Each domain was evaluated as follows: high risk of bias, low risk of bias, and unclear risk of bias.

2.5. Data analysis

We used RevMan 5.3.5 (Cochrane Informatics and Knowledge Management Department; available at http://tech.cochrane.org/revman/download) to conduct the statistical analysis. Dichotomous data were expressed as risk ratio (RR) with 95% confidence interval (CI), whereas continuous data were presented as mean difference (MD) with 95% CIs. We converted other forms of data into either RRs or MDs. We planned to assess heterogeneity using the I^2 statistic to quantify inconsistency among the included studies. An I^2 value > 50% was considered indicative of substantial heterogeneity.[22]

3. Results

3.1. Study selection and description

Our search generated a total of 4956 potentially relevant studies, from which 237 duplicated and 4513 irrelevant studies were excluded after screening the titles and abstracts. Subsequently, 199 full-text articles were reviewed, of which seven met our eligibility criteria. The PRISMA diagram of our search process and study selection is shown in Fig. 1.

The included trials originated from China (n = 6)[23–28] and Russia (n = 1).[29] Six trials were published in Chinese and one trial was published in Russian. All seven studies used parallel groups, but their designs, in terms of allocation method and blinding procedure, were not adequately stated. All included trials involved children less than 18 years of age and a total of 1067 patients were included in these analyses. One trial compared HM with antibiotics,[28] and six trials.[23–27,29] used a combination of HM and conventional therapy for intervention, and conventional therapy as the control. None of trials reported adverse events. The key data from the included studies are summarized in Table 1.

3.2. Risk of bias in the included studies

We attempted to contact the authors of the included studies through