INPLASY

Clinical Status, Efficacy and Safety of Ambroxol Clenbuterol Oral Solution in the Treatment of wheezing disorders in children: Evidence Mapping and Meta Analysis

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None.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 August 2024 and was last updated on 27 August 2024.

INTRODUCTION

Review question / Objective An overview evaluation of the current state of clinical status, efficacy and safety of ambroxol clenbuterol oral solution (ACOS) in the treatment of wheezing disorders in children.

Rationale To provide a general description of the current status of clinical research on ACOS. For example, publication year, regional distribution (province and city), sample size, disease distribution, interventions, and risk of bias assessment. Using Meta-analysis, compare the difference in efficacy between ACOS combo-therapy with conventional therapy vs. conventional therapy.

Condition being studied Wheezing disorders is one of the most common respiratory symptoms in children and often occurs when they have a respiratory diseases. In many childhood respiratory diseases, such as bronchial asthma (asthma), bronchiolitis, and pneumonia, wheezing can be a predominant clinical feature. Data show that about 34% of children have at least one episode of wheezing before the age of 3 years, and nearly half of them will experience wheezing before the age of 6 years.The clinical manifestation of wheezing in children is a persistent, ragged, high-pitched sound during respiration, produced by the formation of turbulence in gases passing through narrow airways. Coughing is the body's defense response against inflammation in the bronchi and lung tissue, but excessive coughing can significantly affect the sleep and quality of life of children. Sputum is an abnormal secretion of local bronchial or lung tissue inflammation, containing mucus, shed cells and cell debris, as well as pathogenic microorganisms. Thick sputum can lead to bronchial obstruction, affecting the ventilation function of lung tissue. Stopping cough and resolving phlegm is an important adjunctive treatment for wheezing in children, which is beneficial for the smooth discharge of phlegm, improving the sleep and quality of life of children.
Commonly used medications for wheezing disorders in children include bronchodilators,

glucose corticosteroids, leukotriene modulators, and antihistamines. Among them, mucus solubilizers need to be used in conjunction with positional drainage, and there is also a risk of causing bronchospasm, so they should be used with caution in children. Mucus regulators are mainly used for children with wheezing diseases. Nausea and irritating expectorants have poor taste, and some children find it difficult to cooperate. Ambroxol Clenbuterol Oral Solution (ACOS) is a compound preparation of ambroxol and clenbuterol. Ambroxol can stimulate the formation of respiratory surfactants, regulate the secretion of serous and mucinous fluids, reduce the surface tension of sputum and adhesion to airway epithelium, promote cilia oscillation, and make sputum easy to cough up. It can also affect the generation and excretion of sputum by promoting anti-inflammatory and antioxidant effects. Clenbutero is β2 receptor agonists help promote ciliary oscillation. ACOS has a good taste, good safety, and can effectively promote sputum discharge. It has been widely used in clinical practice. However, there is currently a lack of comprehensive and high-quality evidence to summarize the clinical benefits and safety of this drug. We will describe and analyze the current available evidence, in order to examine the distribution of evidence and further evaluate the efficacy and safety of ACOS in the treatment of wheezing disorders in children.

METHODS

Search strategy Search conducted on May28, 2024

Pubmed

"chf 023"[tw] OR chf023[tw] OR clembroxol[tw] OR (clenbuterol[tw] AND ambroxol[tw]) OR yitanjing[tw] OR ventoliber[tw] 20

embase

'ambroxol plus clenbuterol'/exp OR ("chf 023" OR chf023 OR clembroxol OR (clenbuterol NEAR/2 ambroxol) OR yitanjing OR ventoliber):ab,ti,kw 24

Cochrane

("chf 023" OR chf023 OR clembroxol OR (clenbuterol NEAR/2 ambroxol) OR yitanjing OR ventoliber):ab,ti,kw 5

Cnki（期刊、学位、会议，中英文扩展：是，中文）

(SU%=氨溴特罗+氨溴索*克仑特罗+易坦静 OR TKA % 氨溴特罗+氨溴索*克仑特罗+易坦静) AND (SU%=儿童+婴儿+幼儿+婴幼儿+少儿+小儿+学龄+学龄前+学生+小学生+早产儿+新生儿+儿科+低龄+适龄+患儿+学龄+小学生+中学生+学生+青少年+少年 OR TKA % 儿童+婴儿+幼儿+婴幼儿+少儿+小儿+学龄+学龄前+学生+小学生+早产儿+新生儿+儿科+低龄+适龄+患儿+学龄+小学生+中学生+学生+青少年+少年) AND (SU%=哮喘+喘息性疾病+喘息性支气管炎+喘支+喘息性+喘息型+喘+咳喘性+咳喘型+哮鸣音+气道炎症+毛细支气管炎+支原体肺炎+支气管肺炎 OR TKA % 哮喘+喘息性疾病+喘息性支气管炎+喘支+喘息性+喘息型+喘+咳喘性+咳喘型+哮鸣音+气道炎症+毛细支气管炎+支原体肺炎+支气管肺炎) 403

万方（期刊、学位、会议）

(主题:("氨溴索" AND "克仑特罗") or 主题:("氨溴特罗" OR "易坦静")) and 主题:(儿童 OR 婴儿 OR 幼儿 OR 婴幼儿 OR 少儿 OR 小儿 OR 学龄 OR 学龄前 OR 学生 OR 小学生 OR 早产儿 OR 新生儿 OR 儿科 OR 低龄 OR 适龄 OR 患儿 OR 学龄 OR 小学生 OR 中学生 OR 学生 OR 青少年 OR 少年) and 主题:("哮喘" OR "喘息" OR "喘支" OR "喘" OR "咳喘" OR "哮鸣音" OR "气道炎症" OR "毛细支气管炎" OR "支原体肺炎" OR "支气管肺炎") 456

CBM

(("氨溴索"[常用字段:智能] AND "克仑特罗"[常用字段:智能]) OR "氨溴特罗"[常用字段:智能] OR "易坦静"[常用字段:智能]) AND ("儿童"[常用字段:智能] OR "婴儿"[常用字段:智能] OR "幼儿"[常用字段:智能] OR "婴幼儿"[常用字段:智能] OR "少儿"[常用字段:智能] OR "小儿"[常用字段:智能] OR "学龄"[常用字段:智能] OR "学龄前"[常用字段:智能] OR "学生"[常用字段:智能] OR "小学生"[常用字段:智能] OR "早产儿"[常用字段:智能] OR "新生儿"[常用字段:智能] OR "儿科"[常用字段:智能] OR "低龄"[常用字段:智能] OR "适龄"[常用字段:智能] OR "患儿"[常用字段:智能] OR "学龄"[常用字段:智能] OR "小学生"[常用字段:智能] OR "中学生"[常用字段:智能] OR "学生"[常用字段:智能] OR "青少年"[常用字段:智能] OR "少年"[常用字段:智能]) AND ("哮喘"[常用字段:智能] OR "喘息性疾病"[常用字段:智能] OR "喘息性支气管炎"[常用字段:智能] OR "喘支"[常用字段:智能] OR "喘息性"[常用字段:智能] OR "喘息型"[常用字段:智能] OR "喘"[常用字段:智能] OR "咳喘性"[常用字段:智能] OR "咳喘型"[常用字段:智能] OR "哮鸣音"[常用字段:智能] OR "气道炎症"[常用字段:智能] OR "毛细支气管炎"[常用字段:智能] OR "支原体肺炎"[常用字段:智能] OR "支气管肺炎"[常用字段:智能]) 401.

Participant or population Age less than or equal to 14 years old. Children diagnosed with wheezing disorders, including those with acute bronchitis, pneumonia, bronchial asthma with infection, and acute infectious bronchiolitis, etc.

Intervention Mappoing: Ambroxol Clenbuterol Oral Solution (ACOS). Not limited to use alone or in combination and frequency of dosage. Meta -analysis: Ambroxol Clenbuterol Oral Solution (ACOS) combo-therapy with conventional therapy.

Comparator Mapping: Other drugs with expectorant properties. 1) Chemicals: Ambroxol oral dosage form, Ambroxol + terbutaline sulphate, general cough suppressant chemicals, guaiacolsulphonic acid potassium syrup, cotrimoxazole oral solution, cotrimoxazole ammonium chloride oral solution, ambroxol + salbutamol, procaterol. 2) Proprietary Chinese medicines: Pediatric Cough Syrup, Lung Li Cough Compound, Syrup of Acute Cough, Pediatric Cough Syrup, Xuan Lung Cough Compound, Jin Zhen Oral Liquid, Pediatric Lung-Heat Cough and Asthma Oral Liquid, Pediatric Cough and Asthma, Pediatric Cough Syrup, Cough Syrup of Eliminating Cum and Relieving Cough. Meta-analysis: Conventional therapy. The article clearly refers to it as “conventional therapy”.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria The literature for Meta-analysis was obtained from core journals. The criterion of core journals is to be included in the Directory of Chinese Science and Technology Core Journals (2023) (Natural Science Volume).

Information sources The identification of included studies, which began on May 28, 2024, will be based on a search strategy performed for each electronic database: three English databases (PubMed; Embase; Cochrane library databases) and three Chinese databases (China National Knowledge Infrastructure, CNKI; Wanfang; China Biology Medicine, Cbm).

Main outcome(s) Mapping: Publication years, region, disease diagnosis, age, intervention and control. Meta-analysis: treatment effectiveness, time to cough disappearance, time to cough sputum disappearance, time to wheeze disappearance.

Additional outcome(s) Meta-analysis: adverse events, such as psychoneurological response (headache, drowsiness, insomnia, numbness of limbs, etc), circulatory system response (increased blood pressure, arrhythmia, etc), allergic reaction and adverse gastrointestinal reaction.

Data management Data will be extracted from papers included in the evidence mapping and meta analysis by two or more independent reviewers using a standardized data extraction form. Any disagreements that arise between the reviewers will be resolved through discussion, or with an additional reviewer/s. If appropriate, authors of papers will be contacted to request missing or additional data, where required.

Quality assessment / Risk of bias analysis The quality of the RCTs was assessed utilizing the Cochrane Risk of Bias tool[12], encompassing sequence generation, allocation concealment, masking of participants and personnel, outcome evaluation concealment, absent result data, and selective result articulation.

Strategy of data synthesis Evidence Mapping: A qualitative summary of the clinical studies conducted using ACOS was performed using statistical descriptive methods, and descriptive analysis was performed using statistical charts and tables.
Meta-analysis: Data was synthesised with a random-effects model considering the clinical and methodological heterogeneity and analysed using RevMan version 5.4 (Review Manager software, Cochrane Collaboration, 2020). For dichotomous results, we computed risk ratios (RRs) along with their 95% confidence intervals (CIs). For continuous results, we calculated mean differences (MDs) accompanied by their 95% CIs.

Subgroup analysis None.

Sensitivity analysis We defined I2 ≥50% with a statistically significant $\chi 2$ test result ($P<0.1$) as evidence of substantial levels of heterogeneity, where I2 measures the proportion of variation that is due to between-study heterogeneity rather than due to chance. Results of statistical heterogeneity were discussed.

Language restriction The literature languages are English and Chinese.

Country(ies) involved China.

Keywords Wheezing disorders; Children; Ambroxol Clenbuterol Oral Solution; Evidence Mapping; Meta analysis.

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