EVIDENCE-BASED INTEGRATIVE MEDICINE

Potassium Dehydroandrographolide Succinate Injection for the Treatment of Child Epidemic Parotitis: A Systematic Review and Meta-Analysis*

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ABSTRACT  Objective: To systematically evaluate the clinical efficacy and safety of Potassium Dehydroandrographolide Succinate Injection (PDSI) in the treatment of child epidemic parotitis (EP). Methods: Randomized controlled trials (RCTs) regarding PDSI in the treatment of child EP were searched in China National Knowledge Infrastructure, Wanfang Database, Chinese Biomedical Literature Database, PubMed, and Cochrane Library from inception to July 30, 2013. Two reviewers independently retrieved RCTs and extracted information. The Cochrane risk of bias method was used to assess the quality of included studies, and a meta-analysis was conducted with RevMan 5.2 software. Results: A total of 11 studies with 818 participants were included. The quality of the studies was generally low, among which only one study mentioned the random method. The meta-analysis indicated that PDSI was more effective than the conventional therapy with Western medicine for EP in the outcomes of the total effective rate [relative risk (RR)=1.23, 95% confidence interval (CI) [1.14, 1.33], P<0.01], the time of temperature return to normal, the time of detumescence [mean difference (MD)=–2.10, 95% CI [-2.78, –1.41], P<0.01], and the incidence of complications (RR=0.14, 95% CI [0.03, 0.72], P=0.02). There were 6 adverse drug reactions (ADRs) in this systematic review, 2 of which were mainly represented rash and diarrhea in the experiment group, while another 4 ADRs occurred in the control group. Conclusions: Based on the systematic review, PDSI was effectiveness and relatively safely in the treatment of child EP. But further rigorously designed trials are warranted to determine its effectiveness.

KEYWORDS Potassium Dehydroandrographolide Succinate Injection, child epidemic parotitis, meta-analysis, systematic review, Chinese medicine

Child epidemic parotitis (EP), a C class infectious disease, is one of the common acute respiratory infectious diseases in children. Its etiology was parotid gland virus, which can spread in the air by saliva or respiratory secretions of the patients and healthy carriers. It also can lead to a variety of glandular tissue, nervous system, liver and other organ damage. However, parotid gland virus was non-sensitive to a variety of antiviral drugs with high infectivity, it is difficult to achieve satisfactory effects with conventional Western medicine (WM).

Recently, Chinese medicine (CM) has played a leading role in the treatment of child EP. The pathogenesis considered in CM is epidemic diseases with wind-heat invading the body. Therefore, the main treatments are expelling wind and heat, detoxification and dissipating. Potassium Dehydroandrographolide Succinate Injection (PDSI) is one of the first batch of essential Chinese patent drugs in the emergency department (room) of national CM hospitals, which was issued by the State Drug Administration of China.

Its effective constituent is dehydroandrographolide succinic acid half ester monopotassium salt, which is synthesized by succinic anhydride and andrographolide. Andrographolide is the main active ingredient extracted from Andrographis paniculata, which is mostly used in the clinical treatment of acute respiratory infections, especially has significant effect on child EP.

Research outcomes based on clinical trials concerning the efficacy of child EP are varying, but meta-analysis in this field is scarce. Therefore, the systematic review aims to evaluate the efficacy and
safety of PDSI in the treatment of child EP, so as to provide a scientific basis for its clinical use.

METHODS

Study Search

Two reviewers (Wu JR and Zhang XM) respectively retrieved the randomized controlled trials (RCTs) that regarding PDSI in the treatment of child EP by searching the following databases from inception to July 30, 2013: China National Knowledge Infrastructure (CNKI), Wanfang Data, Chinese Biomedical Literature Database (CBM), PubMed, and Cochrane Library. Different search strategies were combined as follows: for English databases, MeSH terms as “potassium dehydroandrographolide succinate” and “EP” were used; for Chinese databases, subject terms as “Chuanhuning” and then “Liu Xing Xing Sai Xian Yan” for secondary retrieval were used. Studies published in English or Chinese were considered.

Inclusion Criteria

Studies meeting the following criteria were included. (1) Study type: clinical RCTs used PDSI to treat EP, regardless of blinding. (2) Patient: the diagnostic criterion of child EP conformed to ZHU Fu-tang Practice of Pediatrics. The age of patients was not exceeded 14, while sex and race were not limited. And all the patients had a history of exposure to EP, the temperatures were above 38 ℃, and bilateral or unilateral parotid was swelling and pain. (3) Intervention and comparator measures: the control group was given symptomatic treatment with WM, such as antiviral therapy, sometimes in combination with ribavirin. The experimental group was treated with the same WM as the control group, but combined with PDSI. (4) Outcomes: the primary outcome was the total effective rate, using the following formula: the total effective rate (%) = (number of patients of significantly effective+ number of patients of effective)/ total number of patients × 100%. Significantly effective was determined when temperature returned to normal and cheek swelling subsided in 72 h after treatment. Effective was determined when the time of body temperature return to normal and cheek detumescence was above 72 h. Invalid was determined when the body temperature was still unnormal, cheek swelling was not subsided, and complications appeared after 72-h treatment. Secondary outcomes were the time of temperature return to normal, the time of detumescence, the incidence of complications, and the number of identified adverse drug reactions (ADRs)/adverse drug events (ADEs).

Exclusion Criteria

Studies meeting one of the following phenomena were excluded. (1) Patients had complication of mumps meningitis. (2) CM, acupuncture or surgery was combined used in the control or experimental group.

Data Extraction and Quality Assessment

For the included studies, two reviewers (Wu JR and Zhang XM) independently extracted data of study type, patients’ characteristics, interventions, duration of treatment, outcomes, and methodological quality by using a standard data extraction template. The risk of bias of the included trials was strictly assessed according to the Cochrane risk of bias tool, which included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias. For each item, there were three grades of risk: low risk of bias, unclear, and high risk of bias. When inadequate information was presented in the article and we were unable to explicitly judge “high” or “low”, the item was judged as “unclear”. Wu JR and Zhang XM independently completed and mutually checked the allocated grades. Any disagreements on data extraction and quality assessment were resolved by consensus, or if required by a third reviewer.

Statistical Analysis

To summarize the effects of PDSI for child EP, RevMan 5.2 software was used, whose package was produced and updated by the Nordic Cochrane Centre. Relative risk (RR) was used for dichotomous data, and mean difference (MD) was used for continuous variables, both with 95% confidence interval (CI). \( P<0.05 \) was considered significantly different. The Chi-square test was used for checking the heterogeneity between studies, and \( I^2 \) could show the degree of heterogeneity. If \( P>0.1, I^2<50\% \), it was determined to be little heterogeneity between studies, then a fixed effects model could be used, otherwise a random effects model should be used. Furthermore, groups would be divided into subgroups based on the different kinds of medicines in the control group in clinical. And if the number of included trials was sufficient, a funnel plot would be carried out to assess publication bias. Sensitivity analysis was performed to inspect the stability of the results.