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# TREATING PEDIATRIC ASTHMA WITH HOLISTIC APPROACHES OF TRADITIONAL CHINESE MEDICINE: A RETROSPECTIVE STUDY

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## Abstract

**Background:** Asthma is a chronic disease increasingly found in children. To find more economical and efficient alternatives to treat pediatric asthma, the Bureau of National Health Insurance of Taiwan launched the Traditional Chinese Medicine Holistic Treatment Program (TCMHTP). The effect of traditional Chinese medicine (TCM) holistic treatments on pediatric asthma was evaluated based on data collected from the program.
**Materials and Methods:** A retrospective study was performed by analyzing a dataset from Changhua Christian Hospital, Taiwan, between January 1st, 2006 and December 31st, 2010. Patients aged between 2 and 15 years, who had been diagnosed with asthma, and had participated in the TCMHTP were recruited, whereas those with other severe diseases were excluded. We analyzed the frequency of emergency department visits (EDV), inpatient admission rate (IAR), and length of hospitalization (LH) of the patients, before and after TCM treatments. Spectral analysis of heart rate variability (HRV) was also conducted.
**Results:** Fifty-eight patients were recruited. The average age of the patients receiving TCM treatments was 5.67±3.03 years. The frequency of EDV decreased from 0.94±0.85 to 0.67±1.19 times annually (p=0.095), the annual IAR decreased from 0.62±0.78 to 0.26±0.67 (p=0.002) and the average LH decreased from 3.32±4.25 to 0.80±1.64 (p=0.000) days per year. Parasympathetically mediated HRV decreased significantly from 60.42±15.33 to 54.89±16.45 nu (p=0.016).
**Conclusion:** The present study revealed that an appropriate period of TCM holistic treatment intervention can not only significantly lower exacerbations and hospitalization frequency but also reduce vagal tone in asthmatic children.

**Keywords**
Asthma; Complementary medicine; Traditional Chinese medicine (TCM); Holistic therapies

**Abbreviations:** CAM— complementary and alternative medicine, TCM— traditional Chinese medicine, TCMHTP—Traditional Chinese Medicine Holistic Treatment Program, EDV— emergency department visits IAR— inpatient admission rate, LH— length of hospitalization, EMR— electronic medical record, HRV— heart rate variability

## Introduction

Asthma is a chronic respiratory disease with high prevalence, with approximately 300 million sufferers worldwide (Masoli et al., 2004). According to an investigation by the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three, the prevalence of pediatric asthma has increased in developing countries worldwide

(Asher et al., 2006; Pearce et al., 2007). Furthermore, between 2000 and 2003, 4.9% of children worldwide and 3.2% of children in the Asia Pacific suffered from symptoms of severe asthma (Lai et al., 2009).

In addition to the increase in prevalence, different patterns for hospital admission rates and emergency utilities for pediatric asthma have also been reported in many countries (Crater et al., 2001; MacFaul, 2004; Yeh et al., 2008). The frequency of emergency department visits (EDV) and hospitalizations have commonly been linked to asthma severity (Sears, 2008) and might reflect the level of asthma control (Yeh et al., 2008). Severe asthma is not only life threatening but also consumes huge medical resources. A systematic review article by Bahadori et al. (2009) indicated that the increase in asthma-related costs is closely associated with the severity of asthma.

In Taiwan, asthma prevalence increased from 1.3% to 14.7% between 1974 and 2002 (Yeh et al., 2008). Recently, the prevalence of asthma in Taiwan has shown an annual increase of 13.5% in children aged 6–7 and 13.1% in children aged 13–14 (Pearce et al., 2007). The hospital admission rate for children with asthma increased from 83.9 per 100,000 population to 120.3 per 100,000 population between 1996 and 2002: an increase of 6.5% per year. Meanwhile, the length of hospitalization was 3.6±2.4 days for these children.

Rather than conventional western medical treatment for asthma, many parents choose complementary and alternative medicine (CAM) therapies for their children (Bukutu et al., 2008). Possibly discouraged by the limited treatment effect of conventional western medical therapy for pediatric asthma, it seems more parents are inclined toward CAM therapies (Orhan et al., 2003); for example, in New York City, 65% of the parents of children with asthma chose complementary or alternative therapies to control asthmatic symptoms (Sidora-Arcoleo et al., 2007). In Europe, approximately 30% of patients with allergies have used CAM (Schafer, 2004). Moreover, traditional Chinese medicine (TCM) interventions for control of pediatric asthma play a critical role in Asian countries (Bielory and Lupoli, 1999). A study conducted by Adams et al. (2007) indicated that the combination of conventional western medicine with CAM treatment has the potential improve management of pediatric asthma and patients' quality of life. In Taiwan, a nationwide cohort study conducted by Hung et al. (2014) revealed that asthmatic children seemed to benefit from being treated with integrated TCM. A questionnaire survey conducted in Taiwan also obtained favorable appraisals of TCM treatment of pediatric asthma (Hsieh, Fu Jen Catholic University, master thesis).

In view of the popularity of TCM therapy as an alternative option in Taiwan and the increase in the prevalence of pediatric asthma, the Bureau of National Health Insurance of Taiwan launched the TCM Holistic Treatment Program (TCMHTP) for pediatric asthma in 2006. Children under 15 years of age who have been diagnosed with asthma can participate in this program. This program provides several holistic treatment plans including Chinese herbal remedies, meridian massage, and Chinese herbal paste therapy on acupoints.

However, few reports (Sun, 2009; Chang, China Medical University, master thesis) have demonstrated the efficacy of the TCMHTP and none have revealed any changes in the number of EDV and hospitalizations after patients joined the program. Therefore, the purpose of the present study was to investigate the treatment effect of the TCM intervention in this program by analyzing retrospective data.

## Materials and Methods

### Study Design and Population

This study was conducted at outpatient clinics of Changhua Christian Hospital (CCH), a medical center located in Changhua County in Central Taiwan. The data were collected over a period of 5 years, from January 1st, 2006 to December 31st, 2010. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of CCH (approval serial number: 110307). An electronic medical record (EMR) search was performed to gather the patient data (May et al., 2011).

The inclusion criteria were patients clinically diagnosed with asthma in accordance with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code for asthma (493.xx); those aged from 2 to 15 years at the index date; those who had participated in the TCMHTP, and those with EDV or hospitalization records with a primary diagnosis of asthma or upper-respiratory-infection-related ICD-9-CM codes. The index date was defined as the date of joining the TCMHTP. Patients with catastrophic illnesses, such as congenital metabolic disease, cerebral palsy, systemic autoimmune disease, and malignant neoplasm, were excluded.

To explore the EDV and hospitalization of a general pediatric asthma population, a control group was randomly sampled from the EMR dataset from the same target period with the same criteria as the experimental group excluding participation in the TCMHTP.

Data collected included patient demographics, EDV, number of hospitalizations and length of hospitalization. The heart rate variability (HRV) parameters of the study group, including high frequency (HF), low frequency (LF), and LF/HF, were also obtained. The treatment periods were determined by counting the TCM prescription days. Furthermore, the study group was divided into the following three subgroups to evaluate the appropriate treatment periods of TCMHTP intervention: <4 weeks, 4–12 weeks, and >12 weeks.

### Intervention and Clinical Assessments

In addition to regular conventional western medicine, the study group received TCM holistic treatments: 1. Chinese herbal paste therapy applied to acupoints Feishu (BL13), Pishu (BL20), and Shenshu (BL23) for 2 h each time. The Chinese herbal paste comprised Xi Xin (*Asarum heterotropoides)*, Bai Jie Zi (*Sinapis albae semen*), Gan Jiang (*Rhizoma zingiberis*), Gan Sui (*Radix kansui*), and Yan Hu Suo (*Rhizoma corydalis*); 2. Ten-minute bladder meridian

massage on Back-Shu points (Cabioglu and Arslan, 2008); 3 Chinese herbal remedies after pattern identification by TCM physicians.

Spectral analysis of HRV was conducted in the study group. When the patients participated in the TCMHTP, their HRV was measured using a digital monitor, ANSWatch (Taiwan Department of Health medical device product registration number 001525; Taiwan Scientific Corporation, Taipei, Taiwan), during their first TCM visit. Each patient initially took a 20-min rest and then underwent a 7-min ANSWatch measurement. The data were immediately uploaded to a computer and then reviewed, stored, and analyzed. Thereafter, HRV measurements were performed every 3 months. The primary outcomes of interest were the frequency of EDV, inpatient admission rate (IAR), and length of hospitalization (LH).

**Statistical Analysis**

Descriptive statistics were reported in proportions (with 95% confidence intervals) and means (± standard deviation). Paired t-tests were conducted to assess the significance of differences in frequency of EDV, IAR, and LH between pre- and post-TCMHTP intervention. Variation between sexes was analyzed using the chi-square test. A one-way analysis of variance (ANOVA) was used to examine differences among the groups with various treatment periods. A post-hoc multiple comparison analysis was performed using the Bonferroni test. A p-value <0.05 was considered statistically significant. A change-point analysis was also conducted to investigate the most effective TCM intervention periods.

## Results

Fifty-eight children (14 girls and 44 boys) meeting all inclusion criteria were recruited. The average number of clinical visits of these patients was 14.03 and the mean treatment interval was 1.62 weeks. No side effects such as skin reactions were observed after herbal paste application and no adverse drug reactions were reported during treatment. We also randomly sampled 60 patients receiving only conventional western treatment for asthma as the control group. Table 1 shows the demographic characteristics of these patients. The mean age of the recruited patients was 5.67±3.03 years in the experimental group and 5.82±2.82 years in the control group. No significant difference was observed in age, sex, or comorbidities between the study and control groups.

**Table 1:** Demographics and clinical characteristics

| | Study Group (N=58) | Control Group (N=60) | p-value |
|---|---|---|---|
| Age | 5.67±3.03 | 5.82±2.82 | 0.401 |
| Sex | | | 0.474* |
| Male | 44 (75.9%) | 42 (70%) | |
| Female | 14 (24.1%) | 18 (30%) | |
| Comorbidities | | | 0.851* |
| AR | 42 (72.4%) | 44 (73.3%) | |
| AD | 12 (20.7%) | 16 (26.7%) | |
| AR and AD | 11 (19.0%) | 13 (21.7%) | |
| EDV (times/year) | 0.84±0.74 | 0.36±0.35 | 0.000 |
| IAR (times/year) | 0.53±0.70 | 0.17±0.29 | 0.001 |
| LH (days/year) | 2.06±2.25 | 1.93±2.45 | 0.009 |

Student's independent t-test; *Chi-square test; AD: atopic dermatitis; AR: allergic rhinitis; EDV: emergency department visits; IAR: inpatient admission rate; LH: length of hospitalization

Table 2 shows the clinical characteristics before and after the TCMHTP intervention. The frequency of EDV decreased from 0.94±0.85 to 0.67±1.19 times per year (p=0.095) and the IAR decreased from 0.62±0.78 to 0.26±0.67 times per year (p=0.002). Furthermore, a dramatic improvement occurred in the average LH after the program, decreasing from 3.32±4.25 to 0.80±1.64 days per year (p=0.000).

**Table 2:** Clinical characteristics before and after the TCMHTP intervention

| N=58 | Before | After | p-value |
|---|---|---|---|
| EDV | 0.94±0.85 | 0.67±1.19 | 0.095 |
| IAR | 0.62±0.78 | 0.26±0.67 | 0.002 |
| LH | 3.32±4.25 | 0.80±1.64 | 0.000 |

EDV: emergency department visits; IAR: inpatient admission rate; LH: length of hospitalization.

Table 3 shows that the parasympathetically mediated HRV, at normalized high frequency (HF) power, decreased significantly from 60.42±15.33 to 54.89±16.45 nu (p=0.016) whereas sympathetically mediated HRV, at low frequency (LF) power, rose from 39.53±15.35 to 45.09±11.54 nu. The LF/HF ratio did not differ significantly between pre- and post-TCMHTP intervention (p=0.229).

**Table 3:** HRV parameters before and after the TCMHTP intervention

| | Before | After | p-value |
|---|---|---|---|
| HF (nu) | 60.42±15.33 | 54.89±11.53 | 0.016 |
| LF (nu) | 39.53±15.35 | 45.09±11.54 | 0.016 |
| LF/HF ratio | 1.04±2.11 | 3.18±12.95 | 0.229 |

HF: high frequency; LF: low frequency; nu: normalized unit.

A one-way ANOVA was conducted to compare the three subgroups with different intervention periods, revealing a significant difference in the frequency of EDV ($F_{2,53}$=5.315, p=0.008) and IAR ($F_{2,39}$=3.364, p=0.045), whereas no significant difference in LH ($F_{2,39}$=0.716, p=0.495) was found. Furthermore, the Bonferroni test indicated the subgroup with an intervention period of >12 weeks and the subgroup with an intervention period of 4–12 weeks as significant. Exploiting the efficient cumulative sum control chart method for change-point detection, as proposed by Cheng (2009), we identified a change-point for the periods of TCM treatment courses. Figure 1 shows that the estimated change-point for both of IAR and LH was approximately 15 weeks and that for EDV was approximately 11 weeks. When the study patients were divided into two subgroups, one with a 15-week intervention and one with an intervention shorter than 15 weeks, the former provided clear evidence of greater improvement in asthma exacerbations and hospitalization (p<0.05, Table 4). In summary, an effective TCM treatment course for pediatric asthma should be no shorter than 3 months.

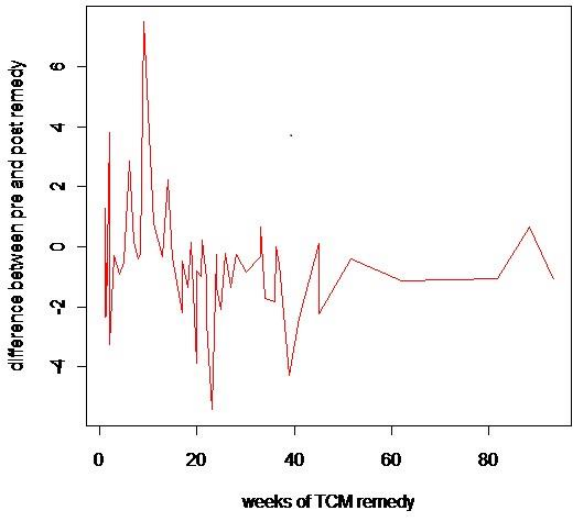


**Figure 1:** Change-point for effective period of treatment

**Table 4:** Clinical characteristics between groups with different intervention periods

| | Intervention Periods | | |
|---|---|---|---|
| | <15 weeks | 15 weeks | p-value |
| | n=21 | n=37 | |
| Age | 5.41±3.50 | 5.81±2.77 | 0.633 |
| ΔEDV | 0.30±1.70 | -0.60±0.71 | 0.007 |
| ΔIAR | -0.41±0.93 | -0.54±0.75 | 0.029 |
| ΔLH | -1.55±3.87 | -3.08±5.07 | 0.202 |

Δ: Change between pre- and post- intervention; EDV: emergency department visits; IAR: inpatient admission rate; LH: length of hospitalization

## Discussion

In our study, far more boys were recruited than girls, which is consistent with a recent International Study of Asthma and Allergies in Children survey conducted in Central Taiwan (Liao et al., 2005; Chiang et al., 2007). Several studies in other countries have also revealed a higher prevalence of asthma in boys than in girls (Bjornson and Mitchell, 2000; Schatz et al., 2006; Tollefsen et al., 2007). In addition, compared with the patients in the control group, the frequency of EDV, IAR, and LH in the experimental group were significantly higher before the TCMHTP intervention. This may have been due to patients being inclined to seek alternative treatment options when conventional western treatment plans fail to effectively control the symptoms of pediatric asthma (Orhan et al., 2003; Torres-Llenza et al., 2010).

According to our results, the frequency of EDV, IAR, and LH improved after adequate intervention periods of holistic TCM treatment. However, climate conditions might have influenced the treatment effect; seasonal trends in asthma exacerbations and hospitalization are widely recognized and Harju et al. (1997) found that peak monthly variations in hospitalization are high in May, autumn, and early winter, whereas they are low in summer and late winter. A Polish study by Stefaniak et al. (2007) described the phenomenon of lower frequency of EDV in summer. Rossi et al. (1991) also indicated seasonal variations in EDV, with rates being the highest in March and the lowest in July. Thus, we conducted a 5-year longitudinal medical survey to minimize the seasonal variations in EDV and hospitalization.

The TCMHTP comprises three types of remedies and the benefits for treating pediatric asthma warrant exploration. Tai et al. (2007) reported that applying TCM herbal paste to acupoints is effective in curing allergy-related diseases. Many recent studies conducted in China have also revealed the effects of acupoint therapy with Chinese herbal paste in curing asthma (Liu et al., 2001; Lai et al., 2001; Sun, 1995). Thus far, the effectiveness and mechanism of manual therapies such as chiropractics and massage remain incompletely understood. A randomized trial by Field et al. (1998) indicated that massage increases the diameter of the airway and improves control of asthma. Regarding TCM herbal remedies, a nationwide population-based study in Taiwan (Huang et al., 2013) identified the 10 most common TCM prescriptions for pediatric asthma. Many other studies have also provided scientific data in various aspects; a randomized, double-blind trial by Chan et al. (2006) showed that Ding-Chuan-Tang, a TCM formula, can reduce airway hyperreactivity in mild to moderate persistent asthma in children. Hsu et al. (2005) reported that another formula, modified Mai-Men-Dong-Tang (MMDT), can improve forced expiratory volume in 1 s (FEV1) and relieve the symptoms of mild to moderate asthma. Another clinical trial by Chang et al. (2006) revealed a significant reduction of symptom scores, total and specific IgE levels, and systemic steroid dose in a group treated with STA-1, a TCM formula composed of MMDT and Liu-Wei-Di-Huang-Wan. Unlike the aforementioned studies, the children who participated in the TCMHTP in our study did not all receive the same specific herbal remedy simultaneously. On the contrary, TCM physicians treated them with individualized prescriptions at each visit, in accordance with the TCM theory of pattern identification. Although the efficacy of individual TCM modalities for asthma remains controversial, TCM is considered a complete and united system and all therapeutic modalities of TCM may contribute to the treatment effect (Yu and Liu, 2010).

Furthermore, TCM is believed to be a favorable alternative option of curing diseases at their roots, although its treatment effect is considered to be slow in action (Lam, 2001). According to our current knowledge, it is doubtful that a longer intervention period would lead to a stronger effect, and the length of an effective TCM treatment course for asthmatic children remains unknown. However, based on the change-point analysis and the data collected in this study, we suggest that a treatment course of approximately 3 months may be necessary for improving pediatric asthmatic symptoms.

In addition to assessing clinical characteristics, a pulmonary function test is considered to be an objective and reliable outcome measurement for asthma. However, obtaining results of high quality and reproducibility is challenging. Testing children without disturbances is difficult, particularly with children younger than 5 years old. Some studies have reported that autonomic dysfunction contributes to the pathophysiology of asthma (Fujii et al., 2000; Garrard et al., 1992; van der Velden and Hulsmann, 1999). HRV reflects autonomic nervous function (ANF) and can serve as a measure of ANF. Regarding the HRV index, HF corresponds to the activities of parasympathetic nerves and LF corresponds to the activities of sympathetic nerves. The ratio of LF to HF (LF/HF) is referred to as the "sympathovagal balance." Compared with that in healthy people, HF in asthmatic patients increases whereas LF decreases. Ostrowska-Nawarycz et al. (2006) suggested that a short-term HRV analysis can be used to assess the autonomic mechanism in the development of bronchial asthma in children and indicated that there is a significant association between the vagal activity in children and the frequency and intensity of bronchial asthma. Kazuma et al. (1997) indicated that even under normal conditions without any asthma attacks, the ANF of asthma patients differs from that of healthy children. Similarly, our results demonstrated that the HRV of the asthmatic children who received TCM treatment was significantly improved.

Despite careful preparation, this study still has limitations. First, this study was conducted by the Department of TCM at CCH, which is the only medical center and main provider of health care in Changhua County in Central Taiwan. In practice, the recruited patients might only be a regional representation, despite the small sample size. Therefore, developing a nationwide survey with health utilization of pediatric asthma treated by TCM will be a critical issue in future studies. Second, the baseline information of conventional western medication use and the contents of TCM prescriptions were unavailable. Third, EMR dataset did not contain information on the socioeconomic status of the patients, and a relationship may exist between asthma and socioeconomic status; Ungar et al. (2011) indicated that children from families with higher annual insurance deductibles have fewer exacerbations. Chen et al. (2006) suggested that children with lower socioeconomic status have worse asthma outcomes. A national birth cohort study may contribute to clarifying this relationship.

## Conclusion

On the basis of a thorough literature review, the present study may be the first to provide an empirical view of how holistic TCM interventions improve pediatric asthma. We suggest that holistic TCM treatment courses of approximately 3 months could significantly reduce exacerbations and hospitalization for children with asthma and vagal tones can become relatively stable. This study constitutes a crucial step in exploring the efficacy of holistic TCM therapies for pediatric asthma so that physicians and parents may be better equipped to make decisions concerning alternative pediatric asthma management.

**Declaration of conflict of interest:** The authors have declared no conflict of interest.

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**Author contributions:** All authors contributed substantially to the conception and design of the study. Prof. Cheng and Dr. Lo performed the majority of the data analysis, and all authors were closely involved in the interpretation of the data. All of the authors participated in drafting or revising the article and approved the final version of the manuscript.

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