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Complementary traditional Chinese medicine use in Children with cerebral palsy: a nationwide retrospective cohort study in Taiwan

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Abstract

Background: Complementary traditional Chinese medicine (TCM) has been used to treat patients with cerebral palsy (CP). However, large-scale surveys examining its use in the treatment of CP and associated disorders are lacking.

Methods: We enrolled 11,218 patients \leq 18 years of age with CP in the Taiwanese National Health Insurance Research Database from 1995 to 2011. Patients were categorized as TCM users ($n = 6,997$; 62.37%) and non-TCM users ($n = 4,221$; 37.63%) based on the inclusion of TCM in their treatment plan.

Results: Children with higher proportions of complementary TCM use were male, younger, and lived in urbanized areas. Most TCM users ($n = 5332$, 76.2%) visited TCM outpatient departments more than 20 times per year. In both groups, the three most common reasons for clinical visits were problems of the nervous system, respiratory system, and digestive system. Acupuncture was commonly used in problems of injury, musculoskeletal system and connective tissue, and nervous system. Chinese herbal medicine was used to improve the primary symptoms of CP in patients, as well as its associated disorders. The incidence rate ratios in allergic rhinitis, dyspepsia, menstrual disorders, and musculoskeletal system and connective tissue diseases among TCM users were significantly higher than non-TCM users. Although patients receiving complementary TCM therapies had higher medical expenditure for utilizing outpatient clinical consultations, their medical costs for visiting ER and hospitalization were significantly lower than that of non-TCM user within one year of the diagnosis of CP.

Conclusion: This study was a large-scale survey to characterize patterns of complementary TCM use among children with CP. The complementary use of TCM in children with CP was considerably high. Future clinical trials and basic researches can be developed based on the findings of this study.

Keywords: Acupuncture, Cerebral palsy, Rehabilitation, Epidemiology, Medical expenditure, National health insurance research database, Traditional Chinese medicine

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Background

Infantile cerebral palsy (CP) refers to a non-progressive syndrome characterized by hypoxia of the underdeveloped brain of infants or children below the age of two (prenatal or perinatal period), thereby inducing postural and motor disabilities [1]. There are many causes of CP, and most cases are believed to be due to prenatal factors. The most common risk factors for CP are prematurity, followed by intrauterine growth restriction, intrauterine infection, antepartum hemorrhage, severe placental pathology, and multiple pregnancy [2]. It is the most common motor disability in childhood with a prevalence of approximately 2 to 4 cases per 1000 children [3].

Current treatment including physical therapy and occupational therapy plays an important role in treating children with CP [4]. In addition to abnormalities of motor activity and posture, children with CP often have other disorders of cerebral function, including intellectual disability or specific learning disabilities, behavioral and emotional disorders, seizures and impaired vision and speech [5]. Therefore, teams consisting of the family and medical staff are necessary to maximize children's social and emotional development, communication, education, nutrition, mobility, and independence in daily activities [6, 7].

The integration of traditional Chinese medicine (TCM) has been widely practiced in Taiwan. It has been used to treat various pediatric diseases such as asthma [8], atopic dermatitis [9], rhinosinusitis [10, 11], diabetes [12], precocity [13], and cancer [14]. A few clinical [15] or animal [16] studies have reported treating CP with TCM, especially by acupuncture. However, there is a lack of large-scale, population-based, epidemiological analyses regarding the utilization patterns of complementary TCM for children with CP.

Since 1995, the majority of the total population in Taiwan (23 million people) has been enrolled in the mandatory National Health Insurance (NHI) program [17]. The practice of TCM has been reimbursed by the NHI program since 1996. Although the broad definition of TCM includes Chinese herbal medicine, proprietary Chinese medicine, acupuncture, moxibustion, manipulation, and Qi management, only the following three major modalities have been covered: (1) Chinese herbal medicine manufactured by GMP-certified pharmaceutical companies (concentrated scientific TCM granules), (2) acupuncture/moxibustion (including acupuncture, moxibustion and cupping therapy) and (3) Chinese orthopedic traumatology therapy (including manipulative therapy, acupressure, and tuina massage) [18]. All claims data were collected in the National Health Insurance Research Database (NHIRD).

We investigated the characteristics of adjunctive TCM use in children with CP by analyzing Taiwan's NHIRD. This dataset comprehensively included all children who

were clinically and radiographically confirmed to have CP with long-term follow-up, thus reducing the potential for sampling bias. This study was important in setting the foundation for understanding the patterns of complementary TCM utilization. The results of this study provided useful information for those involved in the healthcare of children with CP.

Methods

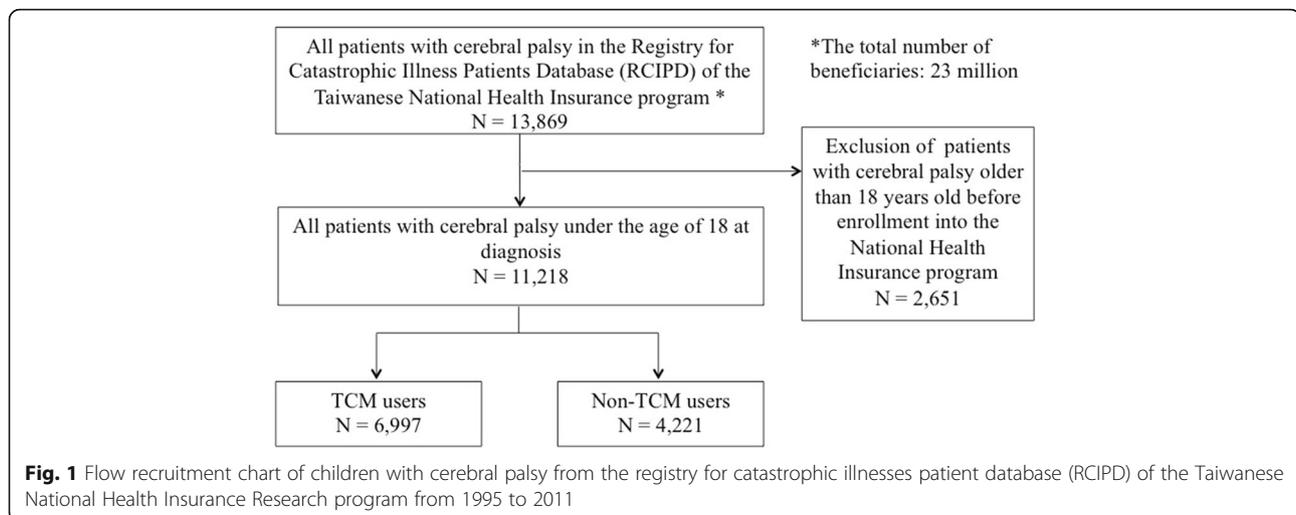
Data source

Taiwan launched the NHI program in March 1995, and by 2015, it covered more than 99% of Taiwanese residents [17]. Since 1995, the NHI program has reimbursed nearly all of the necessary Western medical services and included TCM services in 1996. The choice to utilize TCM or Western medicine belongs to the patient and is not influenced by the insurer. Only licensed TCM doctors are qualified for reimbursement. The large computerized NHI database (NHIRD; <http://nhird.nhri.org.tw/>) was provided by the National Health Insurance Administration and maintained by the National Health Research Institutes of Taiwan. The registry comprises de-identified information regarding medical care facilities, specialties, gender, birth dates, visit dates, prescriptions, health management, costs and diagnostic codes based on the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM). The NHIRD also established a "registry for catastrophic illnesses patient database (RCIPD)", which included approximately 30 disease categories such as cancer, schizophrenia, end-stage renal disease, multiple sclerosis and CP. Catastrophic illness certificates were administered to children with CP who had completed a clinical and neuroimaging evaluation, followed by a thorough and routine review by pediatricians or rehabilitation physicians appointed by the NHI Administration. Thus, the diagnosis of CP in children participating in this study was highly reliable.

Study subjects and variables

The flow chart for the selection of CP cases is illustrated in Fig. 1. Of all 23 million enrollees of the NHI program, patients under the age of 18 ($n = 11,218$) at the time of diagnosis of CP (ICD-9-CM code: 343) in the RCIPD of NHIRD were included in this study. They were then followed-up until the end of 2011. After an accurate diagnosis of CP, the children who consulted with TCM doctors were grouped as TCM users ($n = 6,997$), while the others were grouped as non-TCM users ($n = 4,221$). The demographic characteristics and claims data of this study cohort were collected and analyzed.

The urbanized residential areas of all individuals were divided into two groups, with urban areas more highly represented than rural areas. The urbanization of residential areas has been described previously [19, 20]. In



brief, the residential areas of Taiwan were divided into 4 levels of urbanization based on population density (people/km²), the ratio of the population with varying educational levels, the ratio of elderly people, the ratio of agricultural workers, and the number of physicians per 100,000 people. Levels 1 and 2 of this urbanization were defined as urban areas, while levels 3 and 4 were classified as rural areas.

The concentrated scientific TCM granules included TCM herbal formulas and single herbs. Therapeutic actions and indications of TCM prescriptions were recorded based on the TCM theory [21]. The core prescription patterns were analyzed as described previously [22, 23]. In brief, an open-sourced freeware NodeXL (<http://nodexl.codeplex.com/>) was applied to investigate the core patterns of Chinese herb medicine for the treatment of patients with CP, and the most common two herbal combinations were applied in this network analysis. The thicker line width, defined as counts of connections between formulas and herbs, indicated the more significant prescription patterns in the network.

The medical expenditure of utilizing emergency room (ER) service, outpatient clinical care and hospitalization between patients with and without TCM treatment within one year after CP was diagnosed were calculated in New Taiwan dollars.

Ethics statement

The NHIRD was provided by the National Health Insurance Administration and managed by the National Health Research Institutes, Taiwan. All of the datasets were de-identified and encrypted to protect enrollees' privacy. Therefore, it was not possible to identify individual patients in any way. This study was approved by

the Research Ethics Committee of China Medical University and Hospital (CMUH104-REC2-115).

Statistics

The data were analyzed by using SAS software, version 9.2 (SAS Institute Inc., Cary, NC, U.S.A.). We used the chi-square test to compare categorical variables and the *t*-test to compare continuous variables. We estimated the incidence rate ratio and 95% confidence intervals (CIs) by using the Poisson regression. A *P* value <0.05 was defined as statistically significant.

Results

We identified 11,218 patients under the age of 18 who were diagnosed with infantile CP with catastrophic illness certificates (Fig. 1). Among these children, 62.37% (*n* = 6,997) were TCM users, while 37.63% (*n* = 4,221) were not TCM users. Some proportional differences were found between TCM and non-TCM users in age, sex, urbanization, and annual outpatient clinical visits (Table 1). Children with higher proportions of TCM use were male, younger (age 0–2 and 3–5), and resided in urbanized areas. Furthermore, most TCM users (*n* = 5,332, 76.2%) visited TCM outpatient departments more than 20 times per year. By contrast, the rate of annual outpatient visits was lower in non-TCM users than in TCM users. However, it has to be mentioned that these small differences may not be clinically significant but may be statistically significant given the large sample size.

We further analyzed the frequency distribution of TCM and non-TCM visits by major disease category/diagnosis in children with CP (Table 2). In both groups, the three most common causes of clinical visits were problems of the nervous system (46.6% in TCM users versus 45.6% in non-TCM users), respiratory system

Table 1 Demographic characteristics between TCM and non-TCM users among children with cerebral palsy from 1995–2011

| | TCM user N = 6997 | | Non-TCM user N = 4221 | | p-value |
|---|----------------------|--------|--------------------------|--------|---------|
| | N | % | N | % | |
| Sex ^a | | | | | 0.008 |
| Girl | 2851 | 40.8 | 1827 | 43.3 | |
| Boy | 4146 | 59.3 | 2394 | 56.7 | |
| Age ^a , year | | | | | <0.0001 |
| 0–2 | 3086 | 44.1 | 1444 | 34.2 | |
| 3–5 | 1845 | 26.4 | 896 | 21.2 | |
| 6–12 | 1567 | 22.4 | 1281 | 30.4 | |
| 13–18 | 499 | 7.13 | 600 | 14.2 | |
| Urbanization ^a | | | | | <0.0001 |
| Urban | 4132 | 59.0 | 2322 | 55.0 | |
| Rural | 2865 | 41.0 | 1899 | 45.0 | |
| Annual outpatient clinical visit ^a | | | | | <0.0001 |
| < 5 | 113 | 1.61 | 318 | 7.53 | |
| 5–9 | 386 | 5.52 | 517 | 12.3 | |
| 10–19 | 1166 | 16.7 | 1103 | 26.1 | |
| 20+ | 5332 | 76.2 | 2283 | 54.1 | |
| Mean (SD) ^b | 41.5 | (28.3) | 26.7 | (21.2) | <0.0001 |

^aChi-square test; ^bStudent's t-test

(26.4% in TCM users versus 27.6% in non-TCM users), and digestive system (6.12% in TCM users versus 6.20% in non-TCM users).

We also analyzed the complementary TCM treatment options that the patients received (Table 3). Chinese herbal medicine was mainly used for treating symptoms related to nervous system, respiratory system, signs and ill-defined conditions. Acupuncture was mainly used for treating problems of injury, musculoskeletal system and connective tissue disorder, and nervous system. Chinese orthopedic traumatology was mainly used for symptoms related to nervous system, mental disorder, and injury.

To identify the prescription patterns of TCM doctors in treating children with CP, we also analyzed the Chinese herbal formulas and single herbs prescribed by TCM doctors (Table 4). The most commonly prescribed herbal formula was Ma-Zi-Ren-Wan (4.07%), followed by Liu-Wei-Di-Huang-Wan (3.34%) and Xiang-Sha-Liu-Jun-Zi-Tang (3.27%). The ten most common single herb prescribed by TCM doctors was Rhizoma Acori Graminei (Shi-chang-pu) (2.55%), followed by Radix et Rhizoma Rhei (Da-huang) (2.39%) and Rhizoma Gastrodiae (Tian-ma) (2.1%). The core patterns of Chinese herb medicine for the treatment of patients with CP included Xin-Yi-Qing-Fei-Tang and Radix Glycyrrhizae (Gan-cao) as well as Rhizoma Acori Graminei (Shi-chang-pu), Rhizoma Gastrodiae (Tian-ma) and Radix Polygalae (Yuan-zhi) (Fig. 2).

Table 2 Frequency distribution of TCM and non-TCM visits by disease categories/diagnosis among children with cerebral palsy

| Disease (ICD-9-CM) | TCM user Number of clinical visits = 3214649 | | Non-TCM user Number of clinical visits = 1104382 | |
|--|---|------|---|------|
| | Visits no. | % | Visits no. | % |
| Infectious and parasitic disease (001–139) | 87845 | 2.73 | 50181 | 4.54 |
| Neoplasms (140–239) | 3992 | 0.12 | 1726 | 0.16 |
| Endocrine, nutritional and metabolic disease and immunity disorder (240–279) | 16310 | 0.51 | 5527 | 0.50 |
| Blood and blood-forming organs (280–289) | 2894 | 0.09 | 1208 | 0.11 |
| Mental disorder (290–319) | 195321 | 6.08 | 53797 | 4.87 |
| Nervous system (320–389) | 1496602 | 46.6 | 503782 | 45.6 |
| Circulatory system (390–459) | 21600 | 0.67 | 5241 | 0.47 |
| Respiratory system (460–519) | 847770 | 26.4 | 304833 | 27.6 |
| Digestive system (520–579) | 196656 | 6.12 | 68418 | 6.20 |
| Genitourinary system (580–629) | 16555 | 0.51 | 5870 | 0.53 |
| Complications of pregnancy, childbirth and the puerperium (630–676) | 430 | 0.01 | 74 | 0.01 |
| Skin and subcutaneous tissue (680–709) | 56605 | 1.76 | 24637 | 2.23 |
| Musculoskeletal system and connective tissue (710–739) | 30253 | 0.94 | 7420 | 0.67 |
| Congenital anomalies (740–759) | 56202 | 1.75 | 20061 | 1.82 |
| Certain conditions originating in the perinatal period (760–779) | 26011 | 0.81 | 7171 | 0.65 |
| Symptoms, signs and ill-defined conditions (780–799) | 102187 | 3.18 | 28918 | 2.62 |
| Injury and poisoning (800–999) | 57416 | 1.79 | 15518 | 1.41 |

Table 3 Frequency distribution various TCM therapies by major disease categories/diagnosis among children with cerebral palsy

| Disease (ICD-9-CM) | CHM | COT | ACU | CHM + COT | CHM + ACU | CHM + COT + ACU |
|--|------|------|------|-----------|-----------|-----------------|
| Infectious and parasitic disease (001–139) | 0.38 | 0.31 | 0.10 | 0.73 | 0.13 | 0.35 |
| Neoplasms (140–239) | 0.04 | 0.06 | 0.05 | 0.01 | 0.07 | 0.04 |
| Endocrine, nutritional and metabolic disease and immunity disorder (240–279) | 0.29 | 0.13 | 0.00 | 0.02 | 0.00 | 0.21 |
| Blood and blood-forming organs (280–289) | 0.13 | 0.02 | 0.00 | 0.05 | 0.00 | 0.08 |
| Mental disorder (290–319) | 4.07 | 7.73 | 0.21 | 5.07 | 0.26 | 5.21 |
| Nervous system (320–389) | 31.3 | 76.6 | 22.5 | 67.6 | 27.2 | 47.7 |
| Circulatory system (390–459) | 0.96 | 2.32 | 1.47 | 3.45 | 7.97 | 1.56 |
| Respiratory system (460–519) | 30.6 | 0.79 | 0.00 | 2.88 | 0.26 | 18.2 |
| Digestive system (520–579) | 11.8 | 0.45 | 0.02 | 1.23 | 0.13 | 7.05 |
| Genitourinary system (580–629) | 1.51 | 0.01 | 0.00 | 0.11 | 0.00 | 0.89 |
| Complications of pregnancy, childbirth and the puerperium (630–676) | 0.04 | 0.06 | 0.07 | 0.05 | 0.00 | 0.05 |
| Skin and subcutaneous tissue (680–709) | 1.82 | 0.07 | 0.02 | 0.05 | 0.07 | 1.09 |
| Musculoskeletal system and connective tissue (710–739) | 1.53 | 4.07 | 26.9 | 8.80 | 20.8 | 3.66 |
| Congenital anomalies (740–759) | 0.43 | 1.50 | 1.04 | 1.29 | 0.78 | 0.85 |
| Certain conditions originating in the perinatal period (760–779) | 0.16 | 0.51 | 0.13 | 0.41 | 0.00 | 0.28 |
| Symptoms, signs and ill-defined conditions (780–799) | 14.0 | 0.90 | 0.47 | 2.99 | 0.52 | 8.59 |
| Injury and poisoning (800–999) | 0.90 | 4.47 | 47.0 | 5.25 | 41.9 | 4.19 |

Abbreviations: CHM Chinese herbal medicine, COT Chinese Orthopedic Traumatology, ACU Acupuncture

In a previous study, we found that pediatric TCM users often visited TCM clinics due to the four common diseases: allergic rhinitis, dyspepsia, menstrual disorders, and musculoskeletal system and connective tissue diseases [18]. We further analyzed the prevalence of these four common diseases between children with CP who were TCM users and non-TCM users (Table 5). In all four diseases, the proportions of TCM users were significant higher ($p < 0.0001$) than non-TCM users. Regarding the medical expenditure, complementary TCM users had higher medical expenditure for utilizing outpatient clinical care. However, their medical costs for visiting ER and hospitalization were significantly lower than that of non-TCM user within one year of the diagnosis of CP (Table 6).

Discussion

This population-based study characterized complementary TCM usage among children with cerebral palsy in Taiwan. In this study, we found that the proportion of TCM users in children with CP (62.37%) was much higher than average (22.5%) [18]. Our study was in accordance with a previous study in which younger children with CP used complementary and alternative more frequently [24]. The lower the age of the child with CP, the higher the proportion of TCM utilization that was found. However, this finding was not in agreement with previous studies in which older children with allergic disorders were more likely to consult with TCM services [8–10]. Furthermore, while both TCM users and non-TCM users exhibited high rates of annual outpatient

visits, TCM users showed a higher proportion than non-TCM users. Patients with brain damage need early and comprehensive medical management. In line with some studies' reports on the benefits of treating brain damage or neurological disorders with TCM methods [15, 25, 26], it was quite common in Taiwan to use Chinese medicine to treat children with CP. Compared to other diseases, the utilization of TCM in patients with CP was much higher [18, 27, 28]. Possible reasons for this difference included the following: (1) parents desired a variety of ways to help their ill children, (2) parents' thought that natural products such as Chinese herbs generally had fewer side effects for developing children, and (3) the NHI program covered high-quality Chinese medical outpatient care for children with CP [29, 30], ensuring low medical costs for TCM on the part of the patients.

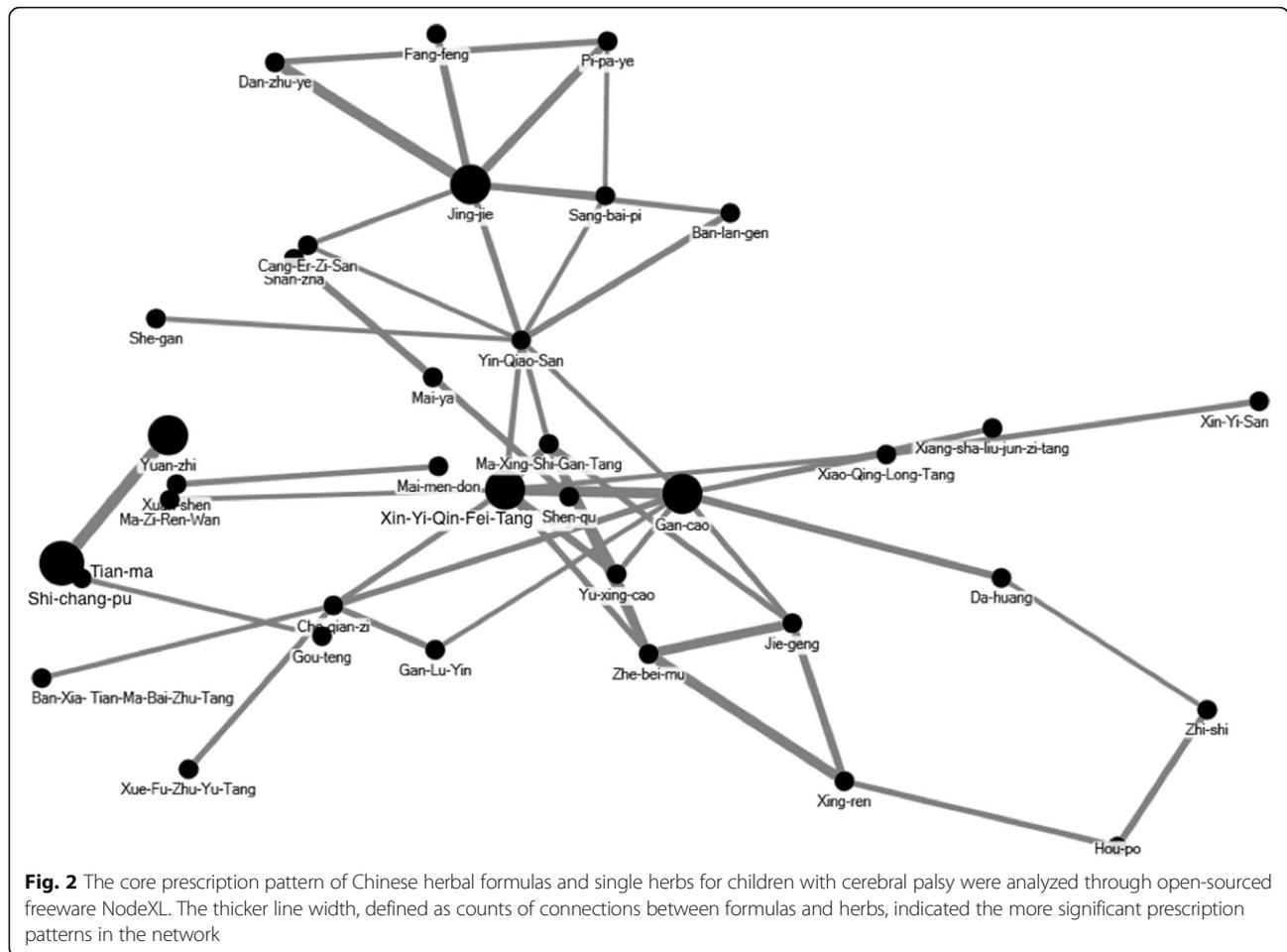
Children with CP often suffer from other disorders of cerebral function, such as intellectual disabilities, neurodevelopmental disorders, epilepsy, visual disorders, and speech and hearing impairments [5]. However, chronic pulmonary disease is a leading cause of death among children with severe CP [31]. The causes of pulmonary disease in these children are recurrent aspiration caused by gastroesophageal reflux and palatopharyngeal incoordination and restrictive disease due to scoliosis [31]. This may have explained why the three most common causes of clinical visits for children with CP in both TCM and non-TCM groups were related to the nervous, respiratory and digestive systems.

Table 4 The common TCM prescription for the treatment of children with cerebral palsy

| Herbal formulas | Pin-yin name | English name | Pin-yin name (Chinese materia medica name; botanical name) | N | % | Daily dose (g) | Average duration (day) |
|-----------------|--------------------------------|--|---|------|------|----------------|------------------------|
| | Ma-Zi-Ren-Wan | Hemp Seed Pill | Huo-ma-ren (Semen Cannabis; <i>Cannabis sativa</i> L.), Xing-ren (Semen Armeniaceae; <i>Prunus armeniaca</i> L.), Bai-shao (Radix Paeoniae Alba; <i>Paeonia lactiflora</i> Pall), Zhi-shi (Fructus Aurantii Immaturus; <i>Citrus × aurantium</i> L.), Hou-po (Cortex Magnoliae; <i>Magnolia hypoleuca</i> Siebold & Zucc.), Da-huang (Radix et Rhizoma Rhei; <i>Rheum palmatum</i> L.), Feng-mi (honey) | 2078 | 4.07 | 8.32 | 2.77 |
| | Liu-Wei-Di-Huang-Wan | Six Ingredient Pill with Rehmannia | Shu-di-huan (Radix Rehmanniae Preparata; <i>Rehmannia glutinosa</i> Gaertn.) Libosch. ex Fisch. & C.A. Mey.), Shan-zhu-yu (Fructus Corni; <i>Cornus officinalis</i> Siebold & Zucc.), Shan-yao (Rhizoma Dioscoreae; <i>Dioscorea opposita</i> Thunb.), Fu-ling (Poria; <i>Wolfiporia cocos</i> (Schw.) Ryv. & Cilbn.), Mu-dan-pi (Cortex Moutan; <i>Paeonia suffruticosa</i> Andr.), Ze-xie (Rhizoma Alismatis; <i>Alisma orientale</i> (Sam.) Juz.) | 1706 | 3.34 | 6.67 | 7.89 |
| | Xiang-Sha-Liu-Jun-Zi-Tang | Six Gentlemen Decoction with Aucklandia and Amomum | Mu-xiang (Radix Aucklandiae; <i>Aucklandia lappa</i> Decne.), Sha-ren (Fructus Amomi; <i>Amomum villosum</i> Lour.), Chen-pi (Pericarpium Citri Reticulatae; <i>Citri Reticulatae</i> Pericarpium), Ban-xia (Rhizoma Pinelliae; <i>Pinellia ternata</i> (Thunb.) Makino), Dang-shan (Radix Codonopsis; <i>Codonopsis pilosula</i> (Franch.) Nannf), Bai-zhu (Rhizoma Atractylodis Macrocephalae; <i>Atractylodes macrocephala</i> Koidz.), Fu-ling (Poria; <i>Wolfiporia cocos</i> (Schw.) Ryv. & Cilbn.), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch.), Sheng-jiang (Rhizoma Zingiberis Recens; <i>Zingiber officinale</i> Roscoe), Da-zao (Fructus Jujubae; <i>Ziziphus jujuba</i> Mill) | 1672 | 3.27 | 8.16 | 4.63 |
| | Shen-Ling-Bai-Zhu-San | Ginseng, Poria and Atractylodis Macrocephalae Powder | Bian-dou (Semen Lablab Album; <i>Lablab purpureus</i> (L.) Sweet), Ren-shen (Radix Ginseng; <i>Panax ginseng</i> C.A.Mey.), Bai-zhu (Rhizoma Atractylodis Macrocephalae; <i>Atractylodes macrocephala</i> Koidz.), Fu-ling (Poria; <i>Wolfiporia cocos</i> (Schw.) Ryv. & Cilbn.), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch.), Shan-yao (Radix Paeoniae Alba; <i>Paeonia lactiflora</i> Pall), Lian-zi (Semen Nelumbinis; <i>Nelumbo nucifera</i> Gaertn.), Yi-yi-ren (Semen Coicis; <i>Coix lacryma-jobi</i> L.), Jie-geng (Radix Platycodonis; <i>Platycodon grandiflorus</i> (Jacq.) A.DC.), Sha-ren (Fructus Amomi; <i>Amomum villosum</i> Lour.), Da-zao (Fructus Jujubae; <i>Ziziphus jujuba</i> Mill) | 1588 | 3.11 | 7.58 | 4.4 |
| | Chai-Hu-Jia-Long-Gu-Mu-Li-Tang | Bupleurum plus Dragon Bone and Oyster Shell Decoction | Chai-hu (Radix Bupleuri; <i>Bupleurum chinense</i> DC.), Huang-qin (Radix Scutellariae; <i>Scutellaria baicalensis</i> Georgi), Ren-shen (Radix Ginseng; <i>Panax ginseng</i> C.A.Mey.), Ban-xia (Rhizoma Pinelliae; <i>Pinellia ternata</i> (Thunb.) Makino), Sheng-jiang (Rhizoma Zingiberis Recens; <i>Zingiber officinale</i> Roscoe), Da-zao (Fructus Jujubae; <i>Ziziphus jujuba</i> Mill.), Fu-ling (Poria; <i>Wolfiporia cocos</i> (Schw.) Ryv. & Cilbn.), Da-huang (Radix et Rhizoma Rhei; <i>Rheum palmatum</i> L.), Mu-li (Concha Ostreae), Qian-dan (Minium) | 1219 | 2.39 | 9.58 | 3.7 |
| | Xin-Yi-Qing-Fei-Tang | Magnolia Flower Drink to Clear the Lungs | Xin-yi (Flos Magnoliae; <i>Magnolia biondii</i> Pamp.), Pi-pa-ye (Fol. Eriobotryae; <i>Eriobotrya japonica</i> (Thunb.) Lindl.), Zhi-zi (Fructus Gardeniae; <i>Gardenia jasminoides</i> J.Ellis), Zhi-mu (Rhizoma Anemarrhenae; <i>Anemarrhena asphodeloides</i> Bunge), Bai-he (Bulbus Lili; <i>Lilium brownii</i> F.E.Br. ex Millez), Huang-qin (Radix Scutellariae; <i>Scutellaria baicalensis</i> Georgi), Sheng-ma (Rhizoma Cimicifugae; <i>Cimicifuga foetida</i> L.), Mai-men-dong (Radix Ophiopogonis; <i>Ophiopogon japonicus</i> (Thunb.) Ker Gawl.), Shi-gao (Gypsum Fibrosum), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch.) | 1209 | 2.37 | 9.02 | 3.04 |
| | Shao-Yao-Gan-Cao-Tang | Peony and Licorice Decoction | Bai-shao (Radix Paeoniae Alba; <i>Paeonia lactiflora</i> Pall), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch.) | 1207 | 2.36 | 7.97 | 6.34 |
| | Ma-Xing-Shi-Gan-Tang | Ephedra, Apricot Kernel, Gypsum and Licorice Decoction | Ma-huang (Herba Ephedrae; <i>Ephedra sinica</i> Stapf), Xing-ren (Semen Armeniaceae; <i>Prunus armeniaca</i> L.), Shi-gao (Gypsum Fibrosum), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch.) | 973 | 1.9 | 7.75 | 8.89 |

Table 4 The common TCM prescription for the treatment of children with cerebral palsy (Continued)

| Xiao-Xu-Ming-Tang | Minor Extend Life Decoction | Ma-huang (Herba Ephedrae; <i>Ephedra sinica</i> Stapf), Chuan-xiong (Rhizoma Chuanxiong); <i>Ligusticum chuanxiong</i> S.H.Qiu, Y.Q.Zeng, K.Y.Pan, Y.C.Tang & J.M.Xu), Han-fang-ji (Radix Stephaniae Tetrandrae; <i>Stephania tetrandra</i> S. Moore), Xing-ren (Semen Armeniacae; <i>Prunus armeniaca</i> L.), Fang-feng (Radix Saposhnikovia; <i>Saposhnikovia divaricata</i> (Turcz.) Schischk.), Sheng-jiang (Rhizoma Zingiberis Recens; <i>Zingiber officinale</i> Roscoe), Ren-shen (Radix Ginseng; <i>Panax ginseng</i> C.A.Mey.), Zhi-fu-zi (Radix Aconiti Lateralis Preparata; <i>Aconitum carmichaeli</i> var. <i>carmichaeli</i>), Gui-zhi (Ramulus Cinnamomi; <i>Cinnamomum cassia</i> (L.) J.Presl), Bai-shao (Radix Paeoniae Alba; <i>Paeonia lactiflora</i> Pall), Huang-qin (Radix Scutellariae; <i>Scutellaria baicalensis</i> Georgi), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch) | 968 | 1.89 | 4.09 | 9.73 |
|----------------------|---|--|------|------|------|------|
| Xiao-jian-Zhong-Tang | Minor Construct the Middle (Burner) Decoction | Yi-tang (Maltose), Gui-zhi (Ramulus Cinnamomi; <i>Cinnamomum cassia</i> (L.) J.Presl), Bai-shao (Radix Paeoniae Alba; <i>Paeonia lactiflora</i> Pall), Sheng-jiang (Rhizoma Zingiberis Recens; <i>Zingiber officinale</i> Roscoe), Gan-cao (Radix Glycyrrhizae; <i>Glycyrrhiza uralensis</i> Fisch), Da-zao (Fructus Jujubae; <i>Ziziphus jujuba</i> Mill) | 966 | 1.89 | 9.16 | 11.2 |
| Single Herbs | Chinese materia medica name | Botanical name | | | | |
| Pin-yin name | | | | | | |
| Shi-chang-pu | Rhizoma Acori Graminei | <i>Acorus tatarinowii</i> Schott | 2212 | 2.55 | 7.12 | 3.59 |
| Da-huang | Radix et Rhizoma Rhei | <i>Rheum palmatum</i> L. | 2067 | 2.39 | 7.71 | 1.99 |
| Tian-ma | Rhizoma Gastrodiae | <i>Gastrodia elata</i> Blume | 1822 | 2.10 | 7.19 | 1.50 |
| Yuan-zhi | Radix Polygalae | <i>Dimocarpus longan</i> Lour | 1778 | 2.05 | 7.89 | 1.17 |
| Gan-cao | Radix Glycyrrhizae | <i>Glycyrrhiza uralensis</i> Fisch | 1724 | 1.99 | 9.16 | 1.45 |
| Zhe-bei-mu | Bulbus Fritillariae Thunbergii | <i>Fritillaria thunbergii</i> Miq. | 1626 | 1.88 | 7.57 | 6.19 |
| Xing-ren | Semen Armeniacae | <i>Prunus armeniaca</i> L. | 1329 | 1.53 | 7.33 | 1.98 |
| Hou-po | Cortex Magnoliae Officinalis | <i>Magnolia hypoleuca</i> Siebold & Zucc | 1238 | 1.43 | 7.98 | 1.96 |
| Jie-geng | Radix Platycodonis | <i>Platycodon grandiflorus</i> (Jacq.) ADC | 1223 | 1.41 | 6.72 | 1.52 |
| Huang-qi | Radix Astragali | <i>Astragalus membranaceus</i> (Fisch.) Bunge | 1059 | 1.22 | 9.14 | 1.71 |



Therefore, children with CP did not only suffer from neurological and musculoskeletal disorders, but the therapy for CP was based on patients' limitations in body structure and function. While medication and/or surgery may have helped to reduce spasticity, hyperreflexia, and clonus, they did not improve weakness and incoordination [32, 33]. Moreover, it was uncertain whether these interventions enhanced functional outcomes. Some reports showed that injections of botulinum toxin type A (BTX A) in combination with physical and occupational therapy improved some functional outcomes [34, 35],

but this treatment did not affect associated disorders such as gastrointestinal and pulmonary dysfunction. Therefore, patients and parents needed to seek other ways to solve these problems. Previous studies also found that children with multiple disabilities chose a wide range of treatments to complement conventional therapies [24, 36]. This may have been another reason for high TCM usage in children with CP.

In Taiwan, the acceptance of acupuncture among children is lower than Chinese herbal medicine [18]. Among the children with CP, we found that many of the patients

Table 5 Incidence rate ratio of diseases between non-TCM and TCM users

| Disease | ICD-9-CM code | TCM user | | Non-TCM user | | Compared to non-TCM user IRR (95% CI) |
|---|---------------|----------|------|--------------|------|---------------------------------------|
| | | N | % | N | % | |
| Allergic rhinitis | 477.9 | 3688 | 52.7 | 1329 | 31.5 | 1.67 (1.57–1.78)*** |
| Dyspepsia and other specified disorders of function of stomach | 536.8 | 2452 | 35.0 | 864 | 20.5 | 1.71 (1.58–1.85)*** |
| Disorders of menstruation and other abnormal bleeding from female genital tract | 626 | 600 | 8.58 | 215 | 5.09 | 1.68 (1.44–1.97)*** |
| Disease of the musculoskeletal system and connective tissue | 710–739 | 5034 | 72.0 | 1977 | 46.8 | 1.54 (1.46–1.62)*** |

IRR incidence rate ratio in Poisson regression

*** p value < 0.0001

Table 6 Total medical expenditure for utilizing ER service, outpatient clinical consultations and hospitalization within one year of diagnosis of cerebral palsy

| Healthcare service | TCM user | | Non-TCM user | | t-test |
|-----------------------------------|-------------------|---------|-------------------|---------|--------|
| | Mean ^a | SD | Mean ^a | SD | |
| ER | 1671.7 | 1591.2 | 1976.1 | 1990.9 | 0.002 |
| Outpatient clinical consultations | 1739.4 | 2267.4 | 891.8 | 1327.0 | 0.03 |
| Hospitalization | 33342.7 | 63914.2 | 46583.5 | 80183.7 | 0.001 |

^aNew Taiwan dollars

received acupuncture or Chinese orthopedic traumatology for symptoms related to injury, musculoskeletal system and connective tissue disorder, mental disorder, and nervous system. The NHI program also fully covered the integrative approaches, including tuina massage (a kind of Chinese orthopedic traumatology methods), ear acupuncture, scalp acupuncture, and somatic acupuncture together to aim to improve the quality of life in children with CP [29]. This provided an option for these children to receive the acupuncture and Chinese orthopedic traumatology.

Among the most common Chinese herbal medicine prescribed for children with CP, majority of them were indicated to treat condition related to the digestive system. Children with CP often have growth failure, which is mainly associated with poor nutrition [37] due to inadequate intake and gastrointestinal abnormalities [37–41]. More than 90 percent of children with CP have clinically significant gastrointestinal symptoms such as swallowing disorders, chronic constipation, regurgitation and/or vomiting, chronic aspiration, and abdominal pain [41]. Furthermore, poor digestive function could lead to chronic pulmonary disease, the main cause of death in these patients [31]. The most commonly prescribed herbal formula in TCM to relieve constipation due to deficient fluid in the colon was Ma-zi-ren-wan, also known as Hemp Seed Pill. In a previous randomized double-blind study, Ma-zi-ren-wan was shown to be safe and effective at alleviating functional constipation [42]. One of the commonly prescribed single herb, Radix et Rhizoma Rhei, was also a commonly used laxative [43]. Other herbal formulas such as Liu-wei-di-huang-wan was used for improving osteoporosis [44] and Shao-yao-gan-cao-tang for relieving muscle spasm [45]. Since neurodevelopmental disorders [46], growth failure [37], orthopedic disorders [47, 48] and osteopenia [49–52] were commonly associated disorders in children with CP, it was reasonable that some of the TCM prescriptions were used for treating these illness. Another category of TCM prescriptions, such as Chai-hu-jia-long-gu-mu-li-tang [21], Rhizoma Acori Graminei [53], Rhizoma Gastrodiae [54] and Radix Polygalae [55], were used for alleviating spasms and regulate the central nervous system. These three herbs were included in the core patterns of Chinese herb medicine

for the treatment of patients with CP. Children with CP were also commonly found to have spastic syndromes [56], dyskinetic syndromes [57], epilepsy [5] and emotional disorders [46]. Various Chinese herbs, such as Xin-Yi-Qing-Fei-Tang, Ma-Xing-Shi-Gan-Tang, Bulbus Fritillariae Thunbergii and Semen Armeniacae, were used for treating respiratory symptoms. Finally, Radix Astragali was used traditionally to raise Qi and has been found to modulate immunity [58]. Taken together, some of the commonly prescribed Chinese herbs were used to complement one another to improve the main symptoms of CP. Others could help treat associated disorders that were not improved by BTX A injection, physical or occupational therapy, such as gastrointestinal and pulmonary dysfunction.

With regard to the rate of TCM and non-TCM use among the four common diseases that we previously found to be prevalent in pediatric TCM users [18], musculoskeletal system and connective tissue diseases had the highest ratio in both groups. The main concerns of patients and parents were likely related to limitations of the body's structure and function. In all four diseases, the proportion of TCM use was significantly higher ($p < 0.0001$) than non-TCM use. This was consistent with our previous study that showed that the rate of TCM use for these four common diseases was higher in children in Taiwan [18].

Interestingly, although the medical expenditure for visiting outpatient clinics within one year of diagnosis of CP of complementary TCM user were higher than the non-TCM users, the medical costs for utilizing ER service and hospitalization were significantly lower. Many parents and policy-makers concerned about the costs of complementary and alternative medicine for patients with CP [59, 60]. This study provided some substantial economic evaluation for the integration of TCM treatment into the clinical healthcare of CP.

Overall, our study provided useful information regarding healthcare and epidemiological patterns of TCM use to treat children with CP. The importance of this study was based on the following aspects: First, based on the literature review and our knowledge, this study was the first large-scale investigation of complementary TCM to patients with CP. Second, this study included all patients below age 18 in the NHIRD with catastrophic illness certificates of CP. The potential for selection bias was eliminated. Third, the NHI system provides low-cost and convenient medical insurance to nearly all residents in Taiwan. Under the NHI program, both Western- and Chinese-based medical resources are very accessible. In 2012, there were approximately 59,017 Western medical doctors and 5,556 licensed TCM doctors serving 23 million people in Taiwan. Moreover, 93.7% of Taiwan's

medical institutions, including hospitals and clinics, take part in the NHI program [61].

The present study had several limitations. First, the NHI system did not reimburse purchases of healthy foods containing herbal ingredients. Second, we were unable to estimate treatment efficacy and disease severity in this study due to the lack of disease severity data in the NHIRD. Lastly, the neuroscience evidence of acupuncture and pharmacological mechanism of Chinese herbal medicine remained unclear. Therefore, we expected future studies and clinical trials to investigate the mechanism and clinical efficacy based on this study.

Conclusion

This study was a large-scale survey to characterize patterns of complementary TCM use among children with CP. The complementary use of TCM in children with CP was considerably high. The reasons for patients' clinical visits were related to their neurodevelopmental and musculoskeletal disorders, as well as their respiratory and digestive system problems. Complementary TCM users had lower medical costs of utilizing ER service and hospitalization than non-TCM users. Future clinical trials and basic researches could be developed based on the findings of this study.

Abbreviations

95% CIs: 95% confidence intervals; BTX A: Botulinum toxin type A; CP: Cerebral palsy; ER: Emergency room; NHI: National health insurance; NHIRD: National health insurance research database; RCPD: Registry for catastrophic illnesses patient database; TCM: Traditional Chinese medicine.

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Availability of data and materials

The datasets we analyzed from NHIRD was provided by the National Health Insurance Administration and maintained by the National Health Research Institutes of Taiwan. The use of NHIRD is limited to research purposes only. Applicants must follow the Computer-Processed Personal Data Protection Law (<http://www.winklerpartners.com/?p=987>) and related regulations of National Health Insurance Administration and National Health Research Institutes.

Authors' contributions

HHL, HRY and TTC conceptualized the study. CHM performed the statistical analysis. HHL, HRY, YCL, MYW, LWC, MFS and TTC contributed to the interpretation of TCM data. LWC contributed to the interpretation of Western

medical data. HHL, MYW, TTC and HRY interpreted the pharmacological mechanisms. HHL, HRY and TTC drafted the manuscript. HRY and TTC finalized the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable in this section.

Ethical approval and consent to participate

This study was approved by the Research Ethics Committee of China Medical University and Hospital (CMUH104-REC2-115) and also the National Health Research Institute, the data holder of the NHI database. The patient consent was exempted for the total animosity of all research data in this study.

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References

1. Van Naarden BK, Doernberg N, Schieve L, Christensen D, Goodman A, Yeargin-Allsopp M. Birth Prevalence of Cerebral Palsy: A Population-Based Study. *Pediatrics*. 2016;137(1):1–9.
2. Strijbis EM, Oudman I, van Essen P, MacLennan AH. Cerebral palsy and the application of the international criteria for acute intrapartum hypoxia. *Obstet Gynecol*. 2006;107(6):1357–65.
3. Johnson A. Prevalence and characteristics of children with cerebral palsy in Europe. *Dev Med Child Neurol*. 2002;44(9):633–640.
4. Russman BS, Tilton A, Gormley Jr ME. Cerebral palsy: a rational approach to a treatment protocol, and the role of botulinum toxin in treatment. *Muscle Nerve Suppl*. 1997;6:S181–193.
5. Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics*. 2012;130(5):e1285–1312.
6. Bagnato SJ, Campbell TF. Comprehensive neurodevelopmental evaluation of children with brain insults. In: Miller G, Ranier JC, editors. *Static Encephalopathies of Infancy and Childhood*. New York: Raven; 1992. p. 27.
7. Zurowski ES. The management of mental retardation. In: Miller G, Ramer JC, editors. *Static Encephalopathies of Infancy and Childhood*. New York: Raven; 1992. p. 119.
8. Huang TP, Liu PH, Lien AS, Yang SL, Chang HH, Yen HR. Characteristics of traditional Chinese medicine use in children with asthma: a nationwide population-based study. *Allergy*. 2013;68(12):1610–3.
9. Lin JF, Liu PH, Huang TP, Lien AS, Ou LS, Yu CH, Yang SL, Chang HH, Yen HR. Characteristics and prescription patterns of traditional Chinese medicine in atopic dermatitis patients: ten-year experiences at a medical center in Taiwan. *Complement Ther Med*. 2014;22(1):141–7.

10. Yen HR, Liang KL, Huang TP, Fan JY, Chang TT, Sun MF. Characteristics of traditional Chinese medicine use for children with allergic rhinitis: a nationwide population-based study. *Int J Pediatr Otorhinolaryngol*. 2015; 79(4):591–7.
11. Yen HR, Sun MF, Lin CL, Sung FC, Wang CC, Liang KL. Adjunctive traditional Chinese medicine therapy for patients with chronic rhinosinusitis: a population-based study. *Int Forum Allergy Rhinol*. 2015;5(3):240–6.
12. Lien AS, Jiang YD, Mou CH, Sun MF, Gau BS, Yen HR. Integrative traditional Chinese medicine therapy reduces the risk of diabetic ketoacidosis in patients with type 1 diabetes mellitus. *J Ethnopharmacol*. 2016;191:324–30.
13. Yu CH, Liu PH, Van YH, Lien AS, Huang TP, Yen HR. Traditional Chinese medicine for idiopathic precocious puberty: A hospital-based retrospective observational study. *Complement Ther Med*. 2014;22(2):258–65.
14. Yen HR, Lai WY, Muo CH, Sun MF. Characteristics of Traditional Chinese Medicine Use in Pediatric Cancer Patients: A Nationwide, Retrospective, Taiwanese-Registry, Population-Based Study. *Integr Cancer Ther*. 2016. doi:10.1177/1534735416659357.
15. Sun JG, Ko CH, Wong V, Sun XR. Randomised control trial of tongue acupuncture versus sham acupuncture in improving functional outcome in cerebral palsy. *J Neurol Neurosurg Psychiatry*. 2004;75(7):1054–7.
16. Zhang Y, Lan R, Wang J, Li XY, Zhu DN, Ma YZ, Wu JT, Liu ZH. Acupuncture reduced apoptosis and up-regulated BDNF and GDNF expression in hippocampus following hypoxia-ischemia in neonatal rats. *J Ethnopharmacol*. 2015;172:124–32.
17. Huang SK. National Health Insurance Annual Report 2015–2016. Taipei: National Health Insurance Administration, Ministry of Health and Welfare; 2015.
18. Huang TP, Liu PH, Lien AS, Yang SL, Chang HH, Yen HR. A nationwide population-based study of traditional Chinese medicine usage in children in Taiwan. *Complement Ther Med*. 2014;22(3):500–10.
19. Liao HH, Yeh CC, Lin CC, Chen BC, Yeh MH, Chang KM, Sun MF, Yen HR. Prescription patterns of Chinese herbal products for patients with fractures in Taiwan: A nationwide population-based study. *J Ethnopharmacol*. 2015; 173:11–9.
20. Liu CYHY, Chuang YL, et al. Incorporating development stratification of Taiwan townships into sampling design of large scale health interview survey. *J Health Manag*. 2006;4:1–22.
21. Scheid V, Bensky D, Ellis A, Barolet R. *Chinese Herbal Medicine: Formulas & Strategies*. 2nd ed. Seattle: Marz; 2009.
22. Chang CM, Chu HT, Wei YH, Chen FP, Wang S, Wu PC, Yen HR, Chen TJ, Chang HH. The Core Pattern Analysis on Chinese Herbal Medicine for Sjogren's syndrome: A Nationwide Population-Based Study. *Sci Rep*. 2015;5:9541.
23. Huang CY, Lai WY, Sun MF, Lin CC, Chen BC, Lin HJ, Chang CM, Yang CH, Huang KC, Yen HR. Prescription Patterns of Traditional Chinese Medicine for Peptic Ulcer Disease in Taiwan: A Nationwide Population-based Study. *J Ethnopharmacol*. 2015. doi:10.1016/j.jep.2015.11.002.
24. Hurvitz EA, Leonard C, Ayyangar R, Nelson VS. Complementary and alternative medicine use in families of children with cerebral palsy. *Dev Med Child Neurol*. 2003;45(6):364–70.
25. Chang CC, Lee YC, Lin CC, Chang CH, Chiu CD, Chou LW, Sun MF, Yen HR. Characteristics of traditional Chinese medicine usage in patients with stroke in Taiwan: A nationwide population-based study. *J Ethnopharmacol*. 2016; 186:311–21.
26. Zheng Y, Zhang ZJ, Han XM, Ding Y, Chen YY, Wang XF, Wei XW, Wang MJ, Cheng Y, Nie ZH, et al. A proprietary herbal medicine (5-Ling Granule) for Tourette syndrome: a randomized controlled trial. *J Child Psychol Psychiatry*. 2015. doi:10.1111/jcpp.12432.
27. Chen FP, Chen TJ, Kung YY, Chen YC, Chou LF, Chen FJ, Hwang SJ. Use frequency of traditional Chinese medicine in Taiwan. *BMC Health Serv Res*. 2007;7:26.
28. Yen HR, Huang TP, Sun MF. Chinese medicine usage in Taiwan: a nationwide population-based study. *RCHM J*. 2013;10:21–7.
29. Chou YT, Yang ST, Wu WH, Lee TY, Chang HH. Current practice of traditional Chinese medicine used in cerebral palsy. *J Chin Med*. 2013;24(1):121–7.
30. Huang IP. A Clinical Appraisal of the High-Quality-Chinese-Medical Outpatient Care Project for Children with Cerebral Palsy: A Case of Hospital Chinese Medicine Outpatient Department. Taoyuan: Chang Gung University; 2008.
31. Reddihough DS, Baikie G, Walstab JE. Cerebral palsy in Victoria, Australia: mortality and causes of death. *J Paediatr Child Health*. 2001;37(2):183–6.
32. Landau WM. Clinical neuromyology II. Parables of palsy pills and PT pedagogy: a spastic dialectic. *Neurology*. 1988;38(9):1496–9.
33. Glenn MB, John W. *The Practical Management of Spasticity in Children and Adults*. Philadelphia: Lea & Febiger; 1990.
34. Tedroff K, Lowing K, Haglund-Akerlind Y, Gutierrez-Farewik E, Forsberg H. Botulinum toxin A treatment in toddlers with cerebral palsy. *Acta Paediatr*. 2010;99(8):1156–62.
35. Hoare BJ, Wallen MA, Imms C, Villanueva E, Rawicki HB, Carey L. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). *Cochrane Database Syst Rev*. 2010;1:CD003469.
36. Bourke-Taylor H, Cotter C, Stephan R. Complementary, Alternative, and Mainstream Service use Among Families with Young Children with Multiple Disabilities: Family Costs to Access Choices. *Phys Occup Ther Pediatr*. 2014. doi:10.3109/01942638.2014.975312.
37. Stallings VA, Charney EB, Davies JC, Cronk CE. Nutritional status and growth of children with diplegic or hemiplegic cerebral palsy. *Dev Med Child Neurol*. 1993;35(11):997–1006.
38. Stevenson RD, Hayes RP, Cater LV, Blackman JA. Clinical correlates of linear growth in children with cerebral palsy. *Dev Med Child Neurol*. 1994;36(2):135–42.
39. Stallings VA, Charney EB, Davies JC, Cronk CE. Nutrition-related growth failure of children with quadriplegic cerebral palsy. *Dev Med Child Neurol*. 1993;35(2):126–38.
40. Sondheimer JM, Morris BA. Gastroesophageal reflux among severely retarded children. *J Pediatr*. 1979;94(5):710–4.
41. Del Giudice E, Staiano A, Capano G, Romano A, Florimonte L, Miele E, Ciarla C, Campanozzi A, Crisanti AF. Gastrointestinal manifestations in children with cerebral palsy. *Brain Dev*. 1999;21(5):307–11.
42. Cheng CW, Bian ZX, Zhu LX, Wu JC, Sung JJ. Efficacy of a Chinese herbal proprietary medicine (Hemp Seed Pill) for functional constipation. *Am J Gastroenterol*. 2011;106(1):120–9.
43. Cirillo C, Capasso R. Constipation and Botanical Medicines: An Overview. *Phytother Res*. 2015;29(10):1488–93.
44. Li M, Wang W, Wang P, Yang K, Sun H, Wang X. The pharmacological effects of morroniside and loganin isolated from *Liuweidihuang* Wan, on MC3T3-E1 cells. *Molecules*. 2010;15(10):7403–14.
45. Hinoshita F, Ogura Y, Suzuki Y, Hara S, Yamada A, Tanaka N, Yamashita A, Marumo F. Effect of orally administered shao-yao-gan-cao-tang (Shakuyaku-kanzo-to) on muscle cramps in maintenance hemodialysis patients: a preliminary study. *Am J Chin Med*. 2003;31(3):445–53.
46. Hurley AD, Sovner R. Psychiatric aspects of cerebral palsy. *Psychiatr Asp Mental Retard Rev*. 1987;6(1):1–5.
47. McCarthy JJ, D'Andrea LP, Betz RR, Clements DH. Scoliosis in the child with cerebral palsy. *J Am Acad Orthop Surg*. 2006;14(6):367–75.
48. Flynn JM, Miller F. Management of hip disorders in patients with cerebral palsy. *J Am Acad Orthop Surg*. 2002;10(3):198–209.
49. Chad KE, McKay HA, Zello GA, Bailey DA, Faulkner RA, Snyder RE. Body composition in nutritionally adequate ambulatory and non-ambulatory children with cerebral palsy and a healthy reference group. *Dev Med Child Neurol*. 2000;42(5):334–9.
50. Henderson RC, Lark RK, Gurka MJ, Worley G, Fung EB, Conaway M, Stallings VA, Stevenson RD. Bone density and metabolism in children and adolescents with moderate to severe cerebral palsy. *Pediatrics*. 2002;110(1 Pt 1):e5.
51. Cohen M, Lahat E, Bistrizter T, Livne A, Heyman E, Rachmiel M. Evidence-based review of bone strength in children and youth with cerebral palsy. *J Child Neurol*. 2009;24(8):959–67.
52. Mergler S, Evenhuis HM, Boot AM, De Man SA, Bindels-De Heus KG, Huijbers WA, Penning C. Epidemiology of low bone mineral density and fractures in children with severe cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2009;51(10):773–8.
53. Zhang H, Han T, Yu CH, Rahman K, Qin LP, Peng C. Ameliorating effects of essential oil from *Acori graminei* rhizoma on learning and memory in aged rats and mice. *J Pharm Pharmacol*. 2007;59(2):301–9.
54. Zhan HD, Zhou HY, Sui YP, Du XL, Wang WH, Dai L, Sui F, Huo HR, Jiang TL. The rhizome of *Gastrodia elata* Blume - An ethnopharmacological review. *J Ethnopharmacol*. 2016;189:361–85.
55. Liu P, Hu Y, Guo DH, Wang DX, Tu HH, Ma L, Xie TT, Kong LY. Potential antidepressant properties of *Radix Polygalae* (Yuan Zhi). *Phytomedicine*. 2010;17(10):794–9.
56. Myklebust BM. A review of myotatic reflexes and the development of motor control and gait in infants and children: a special communication. *Phys Ther*. 1990;70(3):188–203.

57. Menkes JH, Curran J. Clinical and MR correlates in children with extrapyramidal cerebral palsy. *AJNR Am J Neuroradiol.* 1994;15(3):451–7.
58. Fu J, Wang Z, Huang L, Zheng S, Wang D, Chen S, Zhang H, Yang S. Review of the botanical characteristics, phytochemistry, and pharmacology of *Astragalus membranaceus* (Huangqi). *Phytother Res.* 2014;28(9):1275–83.
59. Yoo JE, Yun YJ, Shin YB, Kim NK, Kim SY, Shin MJ, Yu SA. Protocol for a prospective observational study of conventional treatment and traditional Korean medicine combination treatment for children with cerebral palsy. *BMC Complement Altern Med.* 2016;16:172.
60. Wray J, Edwards V, Wyatt K, Maddick A, Logan S, Franck L. Parents' attitudes toward the use of complementary therapy by their children with moderate or severe cerebral palsy. *J Altern Complement Med.* 2014;20(2):130–5.
61. Statistics of General Health. Health Statistical Indices, Taiwan [http://www.mohw.gov.tw/EN/Ministry/Statistic.aspx?f_list_no=474&fod_list_no=4340]. Accessed 28 Nov 2012.

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