Effect of the medication injection site on treatment efficacy in pediatric cerebral palsy: conventional sites vs acupoints

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Abstract

OBJECTIVE: To analyze treatment effectiveness in terms of the medication injection site.

METHODS: The medical records of 423 patients with cerebral palsy who were admitted to Maternal and Child Health Hospital between January 2009 and December 2016 were collected. All cases were divided into T1, T2, T3, and T4 groups based on the use of conventional medication sites and acupoints for administering injectable medicines.

RESULTS: In the T1 group, patients received injections at conventional medication sites between 2009 and 2010. In the T2 group, patients received injections at conventional medication sites combined with acupoint injection therapy I from 2011 to 2012. In the T3 group, injection at conventional medication sites plus acupoint injection II was applied between 2013 and 2014. Acupoint injection only was used in the T4 group from 2015 to 2016. Therapeutic effects were statistically compared among the different injection procedures. The overall Gross Motor Function Measure (GMFM) and Fine Motor Function Measure (FMFM) scores were significantly improved after hospital discharge. The GMFM score was considerably higher in the T4 group than in the other groups (all \( P < 0.05 \)). The GMFM scores were significantly higher in the T2 groups than in the T1 group (\( P < 0.05 \)), but no significant difference was observed between the other paired comparisons (\( P > 0.05 \)). Meanwhile, the FMFM scores were significantly higher in the T2 and T4 groups than in the T1 and T3 groups (all \( P < 0.05 \)). Site injection therapy can significantly improve gross and fine motor function in children with cerebral palsy.

CONCLUSION: It is feasible to administer injectable medicines at acupoints instead of convention sites to enhance the therapeutic effect of treatment in patients with cerebral palsy.

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Keywords: Cerebral palsy; Injections; Acupuncture points; Retrospective studies

INTRODUCTION

Cerebral palsy (CP) comprises a group of persistent syndromes that affect central nervous motor and pos-
tural development and restrain daily activity. These changes are derived from non-progressive damage occurring during fetal or infant brain development. CP is generally accompanied by sensory, cognitive, communication, and behavioral disorders, as well as epilepsy and secondary muscle and skeletal disorders. Preterm birth, low birth weight, asphyxia, and hypoxia are the major causes of pediatric CP. Children diagnosed with CP frequently present with cognitive deficits, auditory or visual disturbances, abnormal behaviors, and epilepsy. These symptoms severely affect physical and mental development, decrease the quality of life of children, and impose a heavy burden on both patients’ families and society. In the rehabilitation department of the Third Affiliated Hospital of Zhengzhou University, the injection of medication at the sites of deficits has been used for decades, and its clinical efficacy has been validated in the treatment of pediatric CP. However, patients must tolerate more pain if the number of injection sites is increased. Balancing the relationship between clinical efficacy and patient pain has been debated in clinical practice.

In this study, the clinical data of patients with CP receiving injection therapy from 2009 to 2016 were collected to compare effectiveness between injection at conventional sites and at acupoints.

**MATERIALS AND METHODS**

**Diagnostic criteria**

The diagnostic criteria of CP, which were established in reference to the 6th National Child Rehabilitation Conference and the 13th National Conference on Pediatric Cerebral Palsy Rehabilitation in April 2014, included the following four aspects: persistent central dyskinesia; abnormal motion and posture development; abnormal development of reflexes; and abnormal muscle tension and strength. According to the symptoms, CP is clinically divided into spastic diplegia, spastic hemiplegia, spastic quadriplegia, dyskinetic CP, ataxic CP, and mixed CP.

**Inclusion criteria**

The eligibility criteria for the study were as follows: age on admission and disease duration between 12 and 24 months; consecutive treatment for three cycles; availability of complete medical records including data for relevant examinations; and willingness to participate in this study and conduct follow-up by telephone.

**Exclusion criteria**

The exclusion criteria of the study were as follows: serious organic diseases, such as diseases of the heart, liver, kidneys, and other vital organs; central nervous system disorders, such as autism, schizophrenia, and epilepsy; severe hearing loss and visual impairment; and spontaneous or persistent hemorrhage after injury. In addition, patients with dyskinetic, ataxic, and mixed CP were excluded because of the small sample sizes.

**Baseline data**

The medical records of 423 children with CP who were admitted to our hospital and discharged after receiving three cycles of treatment between January 2009 and December 2016 were obtained and retrospectively analyzed. All children with CP in this analysis had congenital CP. The course of disease was synchronized with the age of the children. The age, course of disease, gender, and clinical classification of CP of the children were normally distributed, as illustrated in Table 1. One-way analysis of variance (ANOVA) and a multiple-group χ² test revealed no statistical significances in the baseline data among the different groups (all \( P > 0.05 \)). Within 1 week after admission, the Gross Motor Function Measure (GMFM) and Fine Motor Function Measure (FMFM) tests were administered by professors from the rehabilitation department, and the results are presented in Table 2. Because of the large individual differences, the functional scores were not normally distributed. Therefore, the Blom method was utilized to convert the data in normally distributed data, and then the single-factor multi-group χ² test was performed, as shown in Table 3. There were no differences in the total GMFM and FMFM scores on admission among the different groups (all \( P > 0.05 \)).

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases (n)</th>
<th>Age/course of disease (months)</th>
<th>Gender (n)</th>
<th>Cerebral palsy type (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>2009</td>
<td>49</td>
<td>15.1±2.4</td>
<td>31</td>
<td>18</td>
</tr>
<tr>
<td>2010</td>
<td>53</td>
<td>14.5±2.6</td>
<td>33</td>
<td>20</td>
</tr>
<tr>
<td>2011</td>
<td>58</td>
<td>15.4±2.3</td>
<td>37</td>
<td>21</td>
</tr>
<tr>
<td>2012</td>
<td>52</td>
<td>13.8±1.9</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>2013</td>
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<td>15.7±2.4</td>
<td>35</td>
<td>20</td>
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<tr>
<td>2014</td>
<td>51</td>
<td>15.3±2.8</td>
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<tr>
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<td>52</td>
<td>15.1±2.4</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>2016</td>
<td>53</td>
<td>14.6±2.2</td>
<td>32</td>
<td>21</td>
</tr>
</tbody>
</table>
**Observation parameters and therapeutic protocols**

Observation parameters: the GMFM includes 88 items, and it is divided into five functional areas as follows: areas A (lying position and turnover); B (sitting); C (crawling and kneeling); D (standing); and E (walking and running). Each item is evaluated on a scale of 1-4, and the total scores for areas A-E are 51 (17 items), 60 (20 items), 42 (14 items), 39 (13 items), and 72 points (24 items), respectively. Higher scores indicate better gross motor function.

The FMFM scale is divided into five aspects with a total of 45 items, including visual tracking (seven items), upper limb joint mobility (eight items), grasping ability (eight items), operation ability (10 items), and hand-eye coordination ability (12 items). Each item is assessed on a scale of 1-4, and the maximum score is 135 points. Higher scores indicate better fine motor function.

Therapeutic protocols: the treatment protocols consisted of functional training and injection therapy. Functional training was implemented using the Bobath and Vojta methods to inhibit abnormal posture reflexes, suppress abnormal movement, and promote normal motor development. Functional training was performed daily for 1-2 h in each cycle, and one course of treatment lasted 20 d.

Injectable therapy was delivered once every 2 d, and 10 injections were administered in each 20-d course of treatment (Table 4). The injectable medicine consisted of vitamin B1 (100 mL), vitamin B12 (300 mg), monosialotetrahexose ganglioside sodium injection (1 mg), Xingnaojing injection (5 mL), sterile water (4 mL), and 0.9% chlorination sodium (100 mL) sealed at room temperature. Regarding the injection volume, 0.1-0.2 mL of solution was injected into each injection site of the head, 0.3-0.5 mL of solution was delivered to each acupoint of the neck, and the injection volume for the four limbs was determined according to the age and severity of CP. The injection volume for each acupoint was 0.3-0.5 mL.

To reduce injection-induced pain, the injection frequency was gradually reduced over the period of 2009-2016, and the injection sites were gradually replaced by acupoints.

**Injection sites**

In the T1 group, patients received injections at conventional sites between 2009 and 2010. The head consisted of the cerebral cortex motor area, intellectual area, balance area, auditory area, and the area in which the vision area was projected onto the scalp. The limbs included the upper limb deltoid, triceps brachii, ulnar carpal flexor, semi-membrane, semitendinous, gastrocnemius, erector spinae, trapezius, sternocleidomastoid, and other muscles. Each needle was injected into one cm² in the injection area of the head. One intramuscular injection was made per 1 cm following muscles trend. And the injection points formed 1-2 parallel lines. The total number of injections was approximately 160.

In the T2 group, patients received injections at conventional sites combined with acupoint injection therapy I

| Table 2 Evaluation of motor function in children with CP on admission (x ± s) |
|---------------------|------|------|------|------|------|------|------|------|
| GMFM                | 61±9 | 59±10| 59±10| 59±10| 59±9 | 58±10| 57±9 | 59±10|
| FMFM                | 45±10| 45±10| 47±11| 45±10| 48±10| 47±10| 45±9 | 46±10|


| Table 3 ANOVA of motor function scores in children with CP on admission |
|---------------------|------|------|------|------|------|------|------|
| Item                | Sum of squares | df | Mean square | F | Sig. |
| B.GMFM (Between groups) | 395.024 | 395.025 | 415.000 | 0.952 | 0.001 | 1.000 |
| B.FMFM (Between groups) | 391.493 | 391.495 | 415.000 | 0.945 | 0.001 | 1.000 |

Notes: ANOVA: one-way analysis of variance; CP: cerebral palsy; B.GMFM: the Gross Motor Function Measure test was administered before treatment; B.FMFM: the Fine Motor Function Measure test was administered before treatment; df: degree of freedom; F: Fisher value; Sig: significance.

| Table 4 Evaluation of motor function in children with CP at hospital discharge (x ± s) |
|---------------------|------|------|------|------|------|------|------|------|
| GMFM                | 71±11| 68±12| 70±12| 72±10| 70±13| 68±11| 72±10| 73±10|
| FMFM                | 60±10| 58±11| 60±9 | 61±8 | 60±8 | 61±8 | 60±8 | 61±8 |

between 2011 and 2012. The head included Sishencong (EX-HN 1), Baihui (GV 20), the intellectual area, and the area in which the balance area was projected. The limbs included the upper limb deltoid, triceps, ulnar carpi, semi-membrane, semitendinosus, gastrocnemius, erector spinae, trapezius, sternocleidomastoid, and other muscles. Each needle was injected into one cm² in the injection area of the head. Injection was performed in the head at Sishencong and Baihui alone. One intramuscular injection was made per 1 cm² following muscles trend. And the injection points formed 1-2 parallel lines. The total number of injections was approximately 130.

In the T3 group, patients received injections at conventional sites combined with acupoint injection therapy II between 2013 and 2014. The head injection points included Sishencong (EX-HN 1) and Baihui (GV 20). The limb injection points consisted of the upper abdomen deltoid, triceps, gastrocnemius, erector spinae, trapezius, sternocleidomastoid muscles, and acupoints that included Hegu (LI 4), Taichong (LR 3) and Zusani (ST 36). Injection was performed at Sishencong (EX-HN 1), Baihui (GV 20), Hegu (LI 4), Taichong (LR 3) and Zusani (ST 36). One intramuscular injection was made per 1 cm² following muscles trend. And the injection points formed 1-2 parallel lines. The total number of injections was approximately 110.

In the T4 group, patients received acupoint injection therapy between 2015 and 2016. The head acupoints included Sishencong (EX-HN 1) and Baihui (GV 20). The limb acupoints included Neiguan (PC 6), Quchi (LI 11), Jianzhuan (SI 9), Naoshu (SI 10), Tianzong (SI 11), Xiaohai (SI 8), Shouwuli (LI 13), Jianyu (LI 15), Jianliao (TE 14), Naohui (TE 13), Waiguan (TE 5), Tianfu (LU 3), Chize (LU 5), Hegu (LI 4), Zuwuli (LR 10), Yinbai (LR 9), Huantiao (GB 30), Xuanzhong (GB 39), Fengshi (GB 31), Xuehai (SP 10), Ququan (LR 8), Weizhong (BL 40), Zusani (ST 36), Fenglong (ST 40), Chengshan (BL 57), Shenmai (BL 62), and Taichong (LR 3), all of which were double acupoints. The back acupoints included Shenshu (BL 23), Pishu (BL 20), and Weishu (BL 21), all of which were double acupoints. The total number of injections was approximately 70.

**Statistical analysis**

SPSS 22.0 software was used for data processing (IBM Corp., Armonk, NY, USA). If the data were normally distributed, then ANOVA (mean ± standard deviation, x̄ ± s) was directly performed. If the data were not normally distributed, the Blom method was utilized to convert the data into normally distributed data, and then ANOVA (x̄ ± s) was performed. If the test was significant, then the least significant difference test was conducted to assess differences among the groups. P < 0.05 was considered statistically significant.

**RESULTS**

**Improvements of GMFM and FMFM scores after treatment**

Within 1 week before discharge, GMFM and FMFM scores were evaluated by physicians (Table 5). During the period from 2009 to 2016, the GMFM and FMFM scores upon admission and after hospital discharge were recorded and statistically compared, as illustrated in Table 6. The results suggested that the overall GMFM and FMFM scores of children with CP improved after the corresponding injection protocols (all P < 0.05).

**DISCUSSION**

**Therapeutic strategies for CP in Chinese and Western Medicine**

There is no definition of CP in Traditional Chinese Medicine (TCM). Most physicians classify the symptoms and clinical manifestations of CP in the categories of cognitive deficiency, muscle weakness, and stiffness. Some doctors classify the symptoms as spasm, flaccid paralysis, and dementia. Other doctors argue that the entire spectrum of the disease is not reflected

| Table 5 Changes in GMFM and FMFM scores between before and after treatment (x̄ ± s) |
|------------------|------------------|------------------|------------------|
| Item       | T1     | T2     | T3     | T4     |
| GMFM      | 0.001  | 0.082  | 0.001  | 0.060  |
| FMFM      | 0.001  | 0.244  | 0.001  | 0.029  |

Notes: GMFM: the Gross Motor Function Measure; FMFM: the Fine Motor Function Measure; T1: team 1 group; T2: team 2 group; T3: team 3 group; T4: team 4 group.

| Table 6 Least significant difference test of the GMFM and FMFM scores among the different injection groups (P values) |
|------------------|------------------|------------------|------------------|------------------|
| GMFM      | 10.9±4.0  | 9.1±3.6  | 11.2±3.6 | 12.6±2.4 | 11.2±4.8 | 10.4±2.6 | 15.3±3.7 | 14.0±2.7 |
| FMFM      | 14.3±2.7  | 12.6±2.3 | 13.4±3.9 | 15.8±1.9 | 12.9±2.2 | 14.8±3.0 | 15.2±2.0 | 14.9±4.8 |

if CP is defined merely on the basis of its clinical characteristics, 21 they advocate that it should be directly defined as CP in TCM. 3 Nevertheless, TCM practitioners have accumulated a wealth of experience in the clinical diagnosis and treatment of CP. 4,5 In TCM, the treatment approaches mainly include acupuncture, massage, Chinese medicine, fumigation, and moxibustion. Among them, acupuncture has been widely applied in the clinical treatment of CP, and it has displayed favorable clinical efficacy; thus, acupuncture is considered an effective treatment method for CP, and it has received extensive attention and recognition. 6

In Western Medicine, the therapeutic strategies for CP mainly include drug administration; surgical treatment; nerve facilitation technologies, such as proprioceptive neuromuscular facilitation and the Bobath, Brunstrom, Vojta, and Rood approaches; 7,8 basic rehabilitation technology; 9 physical therapy; 10 assistive instrument therapy, 11 and occupational therapy. 12 The injection of medicine at the sites of deficits adopted in the rehabilitation department is considered a medical treatment that is highly similar to acupuncture and moxibustion in TCM. The selection of injection sites also echoes the meridians theory in TCM. Thus, injection therapy can be considered an appropriate treatment for CP in both TCM and Western medicine.

Susceptibility bias
According to the diagnostic criteria of Western medicine, children aged ≥1 year can be diagnosed with CP, whereas brain damage can be diagnosed in children aged <1 year. 3 In addition, some scholars have proposed that early comprehensive rehabilitation therapy can accelerate neurological development and reduce the risk of disability. 13 In this study, there was a minimum interval of 10 days between each course of treatment. Thus, approximately 4 months were required to complete three courses of treatment. Most patients with CP have a strong desire to receive, adhere to, and complete all the therapeutic procedures during the early stage of disease. Therefore, children aged 1-2 years old who experienced relatively short courses of disease and strong therapeutic effects were chosen for this investigation. The diagnosis, evaluation, and treatment procedures were standardized, which could significantly reduce prevalence and control biases.

In addition, because of the age restrictions in the inclusion criteria, susceptibility bias attributable to differences in patient age and the course and severity of disease was significantly minimized. Based on this retrospective survey, the findings possess a certain degree of credibility.

Medication selection
The injection of medicines at sites of deficits has been performed in our hospital for more than 20 years with definite curative effects and an extensive etiology. In addition, the treatment mechanism has also been validated in animal experiments. 14-16 Benign stimulation and drug injection into the head and other sites can repair damaged neurons, improve local tissue metabolism, and relieve muscle spasms. Based on the principle of nurturing nerves, medicine injection in mouse models can promote the maintenance, proliferation, and survival of neurons. 17 Previous studies demonstrated that vitamin B1 can activate the Akt/mTOR/STAT3 signaling pathway and protect against glutamate-induced neuronal injury. 18 As an important coenzyme for methyl transfer reactions, vitamin B12 also plays a pivotal role in maintaining nerve function. 19

Acupoint selection
During the treatment process, the motor area selected as an injection site partially overlaps with parts of the Baihui and Sishencong acupoints. The limb injection sites overlap with the Jianyu, Shouwuli, Quchi, Hegu, Huantiao, Zusanli, Fenglong, Yanglingquan, Chengshan, and Taichong acupoints. The back injection sites coincide with the Beishu acupoint. Acupoints can be selected according to clinical practice combined with theory in TCM. According to the Compendium of Acupuncture and Moxibustion, Baihui is the acupoint for treating stroke, speech obscurity, mouth opening, hemiplegia, upset, nausea, convulsion, insomnia, and other diseases. Hegu and Taichong are the original acupoints of Shouyangming and Zuqueyin, which regulate the gasification function. 20 Sishencong surrounds the Baihui acupoint, which is the site at which the Yang gas aggregates. The anterior and posterior acupoints of Sishencong are located on the meridians, and the left and right acupoints surrounding Sishencong are proximal to the urinary bladder channel, which is linked to the brain through the kidneys. Thus, Sishencong protects the brain and nurtures the kidneys and bone marrow. According to the Huang Di Nei Jing, the Zutaiyang and Guozhong acupoints are acupunctured to bleeding to treat spastic paralysis. Although the theoretical systems of Chinese and Western Medicine are different, the injection route and sites in the treatment of CP are similar. In this study, treatment at acupoints in TCM was associated with a significantly smaller number of injections than Western Medicine. Regarding the therapeutic effect, medicine injection traditional Chinese acupoints was associated with greater clinical efficacy than the other injection protocols. Based on the strong therapeutic effects, it is suggested that injection at acupoints can replace conventional injection therapy in the treatment of CP.

Expectation
Because the collected medical records were written in the Western Medicine pattern, the type of CP could not be further classified according to the TCM theory. Consequently, the selection of acupoints was based on empirical experience.
In subsequent research, it is recommended to integrate dialectical TCM therapies, such as acupuncture and
remedy techniques to widen the scope of treatment and reduce individual differences. In TCM, CP is classified into different categories. However, no consensus regarding classification standards has been reached. In this investigation, patients with dyskinetic, ataxic, and mixed CP were excluded because of their small sample numbers. Thus, only children diagnosed with spastic CP were recruited, which limits the clinical significance of this study. We noticed that the injection sites were completely replaced by acupoints after 2015.

In conclusion, the therapeutic effect of CP treatment could be improved by replacing conventional injection sites with acupoints.

REFERENCES


