Zheng S, Luo Q, Peng L, *et al*. Effect and mechanism of application in canicular days plus enteral nutrition for cough variant asthma in kids. J Acupunct Tuina Sci, 2016, 14(5): 333-339
DOI: 10.1007/s11726-016-0945-z

**Special Topic Study**

# Effect and mechanism of application in canicular days plus enteral nutrition for cough variant asthma in kids

## 三伏灸配合肠内营养治疗儿童咳嗽变异性哮喘的效应与机制研究

Zheng Su (郑苏), Luo Qiang (罗强), Peng Li (彭力), Xu Jing (胥婧), Mu Jing-ping (穆敬平)
Taihe Hospital of Shiyan City Affiliated to Hubei University of Medicine, Hubei Province, Shiyan 442000, China

**Abstract**

**Objective:** To observe the clinical efficacy of application in canicular days plus enteral nutrition in treating cough variant asthma (CVA) in kids, and to explore its action mechanism.

**Methods:** Following a randomized controlled single-blind parallel-group design, 138 eligible kids with CVA were randomized into an observation group, a canicular-day application group, and an enteral nutrition group, 46 kids in each group. The canicular-day application group was intervened by application in canicular days, the enteral nutrition group was by enteral feeding, and the observation group was by both canicular-day application and enteral feeding. The therapeutic efficacies were evaluated after a treatment course.

**Results:** The recovery rate and total effective rate were respectively 50.0% and 98.0% in the observation group, versus 23.9% and 91.3% in the canicular-day application group, and 13.0% and 78.6% in the enteral nutrition group. The observation group was significantly superior to the other two groups (both $P<0.05$). In comparing the global symptom score, peak expiratory flow (PEF), forced expiratory volume in one second (FEV1), $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, $CD8^+$, hemoglobin (Hb), total protein (TP), albumin (ALB), eosinophil cationic protein (ECP), lipid peroxide (LPO), leukotriene (LT), body weight (BW), triceps skin-fold (TSF), and arm muscle circumference (AMC), the observation group was significantly better than the other two groups (both $P<0.05$).

**Conclusion:** Application in canicular days plus enteral nutrition can significantly improve the pulmonary function and symptoms in children's CVA, and the effect is possibly produced by regulating cellular immune system, enhancing Hb, TP, ALB, BW, TSF, AMC, and inhibiting the production of ECP, LPO, and LT.

**Keywords:** Moxibustion Therapy; Cough; Asthma; Enteral Nutrition; Randomized Controlled Trials; Respiratory Function Tests; Child

**【摘要】目的：**观察三伏灸配合肠内营养治疗儿童咳嗽变异性哮喘(cough variant asthma, CVA)的临床疗效，并探讨其作用机制。**方法：**采用随机、单盲、平行对照的原则将符合纳入标准的 138 例 CVA 患儿分为观察组、三伏灸组和肠内营养组，每组 46 例。三伏灸组给与三伏灸治疗，肠内营养组给与肠内营养治疗，观察组给与三伏灸配合肠内营养治疗。治疗 1 个疗程后进行疗效评定。**结果：**观察组治愈率 50.0%，总有效率为 98.0%；三伏灸组治愈率为 23.9%，总有效率为 91.3%；肠内营养组治愈率为 13.0%，总有效率为 78.6%；观察组均明显优于其他两组，差异均有统计学意义(均 $P<0.05$)。在症状总积分、最大呼气流量(peak expiratory flow, PEF)、一秒用力呼气容积(forced expiratory volume in one second, FEV1)、$CD3^+$、$CD4^+$、$CD4^+/CD8^+$和 $CD8^+$、血红蛋白(hemoglobin, Hb)、血清总蛋白(total protein, TP)、清蛋白(albumin, ALB)、嗜酸细胞阳离子蛋白(eosinophil cationic protein, ECP)、过氧化脂质(lipid peroxide, LPO)、白三烯(leukotriene, LT)、体质量、肱三头肌皮皱厚度和上臂肌围上，观察组均优于其他两组，差异均有统计学意义(均 $P<0.05$)。**结论：**三伏灸配合肠内营养能明显改善小儿 CVA 患者的肺功能和临床症状，可能通过调节细胞免疫，提高患者的 Hb、TP、ALB、体质量、肱三头肌皮皱厚度和上臂肌围等营养状况，抑制 ECP、LPO 和 LT 的分泌等机制发挥治疗作用。

**【关键词】**灸法；咳嗽；哮喘；肠营养；随机对照试验；呼吸功能试验；儿童
**【中图分类号】**R245.8　　**【文献标志码】**A

As a special type of asthma severely endangering children's health, cough variant asthma (CVA) is quite common in China. If left untreated, CVA can be recurrent and refractory, and will probably become typical asthma, not only affecting the development and health of the kid, but also bringing huge trouble and burden to the family. Cough often increases the

**Author**: Zheng Su, M.M., physician
**Corresponding Author**: Peng Li, M.D., chief physician, associate professor.
E-mail: liypenghhh@126.com

consumption of energy and gastrointestinal dysfunction usually causes denutrition, which will in turn aggravate the dysfunction of the body, making it more difficult to control CVA[1].

This study was to observe the clinical efficacy of application in canicular days plus enteral nutrition in treating CVA, and to reveal its action mechanism from eosinophil cationic protein (ECP), lipid peroxidation (LPO), $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, $CD8^+$, hemoglobin (Hb), serum total protein (TP), albumin (ALB), and leukotriene (LT).

## 1 Clinical Materials

### 1.1 Diagnostic criteria

The diagnosis was made based on the *Diagnosis and Treatment Guidance of Cough* stipulated by the Asthma Group of Chinese Thoracic Society in 2009[2]: consistent cough or repeated attack over 1 month, usually flared up at night and/or in the morning, aggravated after sports or confronting cold air, with few sputum, no sign of infection, or didn't respond to long-term use of antibiotics; airway hyperresponsiveness, positive bronchial provocation test (BPT) and bronchial dilation test (BDT) or day-night variation of the peak expiratory flow (PEF) over 20%; bronchodilators and glucocorticoid were effective; there was a personal or a family history of allergy, or a family history of asthma, and the allergen test showed positive; cough induced by the following conditions was excluded, including infection with tubercle bacillus, infection with mycoplasma, foreign body in air passage, esophageal reflux, and megalothymus.

### 1.2 Inclusion criteria

Conforming to the above diagnostic criteria; age 8-12 years old; the guardian of the patient signed the informed consent form.

### 1.3 Exclusion criteria

Coupled with other internal diseases that can cause malnutrition, including diabetes, hyperthyroidism, and chronic malabsorption; allergic to the medication used in the application treatment; those with poor compliance.

### 1.4 Statistical method

The SPSS 18.0 version statistical software was adopted for data analyses. According to the test for homogeneity of variance, the measurement data conforming to homogeneity were expressed as mean ± standard deviation ($\bar{x} \pm s$), the inter-group comparisons were analyzed by one-way ANOVA, and the ranked data were by the rank-sum test. $P<0.05$ was considered to have a statistical significance.

### 1.5 General data

Totally 138 subjects were all diagnosed with CVA and recruited from the Pediatrics Department of our hospital, and there were no dropouts during the whole study. They were allocated into 3 groups by using a randomized controlled single-blind parallel-group design: an observation group, a canicular-day application group, and an enteral nutrition group. There were no significant differences in comparing the baseline data among the three groups ($P>0.05$), indicating the comparability (Table 1).

**Table 1. Comparison of general data**

| Group | *n* | Gender (case) | | Average age ($\bar{x} \pm s$, year) |
|---|---|---|---|---|
| | | Male | Female | |
| Observation | 46 | 23 | 23 | 10.0±2.1 |
| Canicular-day application | 46 | 22 | 24 | 10.2±2.0 |
| Enteral nutrition | 46 | 24 | 22 | 10.3±2.0 |

## 2 Treatment Methods

Conventional medication treatment was not adopted in the three groups.

### 2.1 Observation group

#### 2.1.1 Canicular-day application

Points: Dazhui (GV 14), bilateral Dingchuan (EX-B 1), Jingbailao (EX-HN 15), bilateral Feishu (BL 13), Shenshu (BL 23), Gaohuang (BL 43) and Pishu (BL 20).

Operation: *Xi Xin* (*Herba Asari*), *Bai Jie Zi* (*Semen Brassicae*), *Gan Sui* (*Radix Kansui*), *Shu Fu Zi* (*Radix Aconiti Laterails Preparata*), *Yan Hu Suo* (*Rhizoma Corydalis*), and *Zhi Ban Xia* (*Rhizoma Pinelliae Preparata*) (mixed at 4:4:1:1:1:1) were ground into powder and made into herbal cakes (1 cm × 1 cm × 1 cm) when mixed with ginger juice. The cake was placed on a piece of fabric plaster (4 cm × 5 cm) and then applied onto the above points one by one. Each time, 6-7 points from one side of the body were treated, lasting 4-8 h. The plasters shouldn't be pressed or squeezed during the application. One treatment was given in each of the three periods of the canicular days, and the three sessions made a treatment course.

#### 2.1.2 Enteral nutrition

The patients all received indwelling nasogastric tube. On the 1st day, patients were given intravenous (i.v.) 0.9% normal saline or 5% glucose solution 500 mL, lasting for 24 h. On the 2nd day, the enteral nutritional suspension (*Neng Quan Li*, 500 mL/bottle, approval No.: H20010284, NUTRICIA, China) 500 mL was administered at a constant rate, 30-40 mL/h, lasting for 24 h. On the 3rd day, the enteral polymeric feeding was added to 1 500-2 000 mL/d based on the body weight (BW)[3]. The enteral polymeric feeding should be properly warmed and administered via enteral nutrition pumps at a constant rate. After 1-week treatment, the tube feeding would be replaced by oral administration, which lasted for 3 weeks.

 

Caution: Prior to the indwelling of the nasogastric tube, the doctor had to ask whether there were any contraindications, such as nasopharyngeal, esophageal, or gastric diseases or surgery, and basal fracture. During intubation, the doctor had to pay attention to the patient's body signs, and remove the tube immediately when cough, difficulty breathing, or cyanosis occurred. The intubation was performed again when the patient's condition became stable. To avoid laryngeal edema, to patients who suffered repeated failure in intubation, the operation should be performed again 4 h later and better under laryngoscope. Before nasogastric intubation, the doctor had to have a conversation with the patient's guardian and had him or her sign the consent; a polyurethane nasogastric tube can serve 42 d maximum.

**2.2 Canicular-day application group**

The canicular-day application group only received the same application treatment as that used in the observation group.

**2.3 Enteral nutrition group**

The enteral nutrition group only received the same enteral nutrition treatment.

The therapeutic efficacies were evaluated after 3-week treatment.

## 3 Therapeutic Efficacy Observation

**3.1 Observation items**

3.1.1 Symptom and sign score

It was scored according to the criteria of the symptoms and signs of cough from the *Quantized Diagnosis of Traditional Chinese Medicine*[4].

Cough: No cough scored 0 point; mild cough (intermittent, not affecting sleep) scored 1 point; moderate cough (in between the mild cough and severe cough) scored 2 points; severe cough (chronic frequent cough, affecting sleep) scored 3 points.

Sputum amount: No sputum scored 0 point; a small amount (24 h sputum amount ＜5 mL) scored 1 point; moderate amount (24 h sputum amount 6-20 mL) scored 2 points; a large amount (24 h sputum amount ＞20 mL) scored 3 points.

3.1.2 Pulmonary function test[5]

The pulmonary function was measured before and after the treatment to record the peak expiratory flow (PEF) and the forced expiratory volume in 1 s (FEV1).

3.1.3 Blood biochemical items

Venous blood was withdrawn before and after the treatment, and examined by the examination center of our hospital. The major targets included $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, $CD8^+$, hemoglobin (Bb), total protein (TP), albumin (ALB), eosinophil cationic protein (ECP), lipid peroxide (LPO), and leukotriene (LT).

3.1.4 Body test

The BW, triceps skin-fold (TSF), and arm muscle circumference (AMC) were measured before and after the treatment.

**3.2 Criteria of therapeutic efficacy**

It was based on the criteria of therapeutic efficacy of cough from the C*riteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine*[6].

Recovery: Cough was completely gone.

Markedly effective: Cough was significantly improved, and was gone in the morning and at night.

Improved: Cough was slightly improved, but still flared up at night or in the morning.

Invalid: Cough was not improved.

**3.3 Treatment results**

3.3.1 Comparison of clinical efficacies

The recovery rate and total effective rate were respectively 50.0% and 98.0% in the observation group, versus 23.9% and 91.3% in the canicular-day application group, 13.0% and 78.6% in the enteral nutrition group. The recovery rate and total effective rate of the observation group were significantly higher than those of the other two groups ($P<0.05$); the recovery rate and total effective rate of the canicular-day application group were significantly higher than those of the enteral nutrition group ($P<0.05$), (Table 2).

**Table 2. Comparison of clinical efficacies (case)**

| Group | *n* | Recovery | Markedly effective | Improved | Invalid | Recovery rate (%) | Total effective rate (%) |
|---|---|---|---|---|---|---|---|
| Observation | 46 | 23 | 10 | 11 | 2 | 50.0[1)] | 95.7[1)] |
| Canicular-day application | 46 | 11 | 13 | 18 | 4 | 23.9[2)] | 91.3[2)] |
| Enteral nutrition | 46 | 6 | 10 | 20 | 10 | 13.0 | 78.6 |

Note: Compared with the canicular-day application group and the enteral nutrition group, 1) $P<0.05$; compared with the enteral nutrition group, 2) $P<0.05$

3.3.2 Comparison of symptom scores

After the treatment, the global symptom scores were significantly changed in the three groups ($P<0.05$); the score of the observation group was markedly lower than that of the other two groups ($P<0.05$); the score of the canicular-day application group was significantly lower than that of the enteral nutrition group ($P<0.05$), (Table 3).

**Table 3. Comparison of symptom scores ( $\bar{x}$ ±s, point)**

| Group | *n* | Pre-treatment | Post-treatment |
|---|---|---|---|
| Observation | 46 | 25.6±6.3 | 4.8±3.2[1)2)] |
| Canicular-day application | 46 | 25.4±6.1 | 12.5±4.7[1)3)] |
| Enteral nutrition | 46 | 25.8±5.9 | 18.1±5.3[1)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and the enteral nutrition group, 2) $P<0.05$; compared with the enteral nutrition group, 3) $P<0.05$

3.3.3 Comparison of pulmonary function

After the intervention, the PEF and FEV1 values were significantly improved in the three groups ($P<0.05$); the PEF and FEV1 values of the observation group were significantly higher than that of the canicular-day application group and enteral nutrition group ($P<0.05$); the PEF and FEV1 values of the canicular-day application group were markedly better than that of the enteral nutrition group ($P<0.05$), (Table 4).

3.3.4 Comparison of cellular immunity items

Before the treatment, there were no significant inter-group differences in comparing $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, and $CD8^+$ levels ($P>0.05$). After the treatment, the $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, and $CD8^+$ levels were significantly changed in the three groups ($P<0.05$); in the observation group, the $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ levels markedly increased while the $CD8^+$ level markedly decreased, and the results were significantly different from that of the canicular-day application group and the enteral nutrition group ($P<0.05$); the differences were statistically insignificant between the canicular-day application group and the enteral nutrition group ($P>0.05$), (Table 5).

3.3.5 Comparison of blood biochemical items

Before the treatment, there were no significant inter-group differences in comparing the Hb, TP, and ALB contents ($P>0.05$). After the treatment, the Hb, TP, and ALB levels were significantly changed in the three groups ($P<0.05$); the Hb, TP, and ALB contents of the observation group were significantly superior to that of the other two groups ($P<0.05$); the differences were also statistically significant between the canicular-day application group and the enteral nutrition group ($P<0.05$), (Table 6).

3.3.6 Comparison of ECP, LPO, and LT

Before the treatment, there were no significant inter-group differences in comparing the ECP, LPO, and LT contents ($P>0.05$). After the treatment, the ECP, LPO, and LT levels were significantly changed in the three groups ($P<0.05$); the ECP, LPO, and LT contents of the observation group were significantly superior to that of the other two groups ($P<0.05$); the differences were also statistically significant between the canicular-day application group and the enteral nutrition group ($P<0.05$), (Table 7).

3.3.7 Comparison of body measurement

Before the treatment, there were no significant inter-group differences in comparing the BW, TSF, and AMC ($P>0.05$). After the treatment, the BW, TSF, and AMC were significantly changed in the three groups ($P<0.05$); the BW, TSF, and AMC of the observation group were significantly superior to that of the other two groups ($P<0.05$); the differences were also statistically significant between the canicular-day application group and the enteral nutrition group ($P<0.05$), (Table 8).

**Table 4. Comparison of pulmonary function ( $\bar{x}$ ±s, %)**

| Group | *n* | PEF | | FEV1 | |
|---|---|---|---|---|---|
| | | Pre-treatment | Post-treatment | Pre-treatment | Post-treatment |
| Observation | 46 | 72.5±11.2 | 91.2±8.3[1)2)] | 64.2±7.1 | 95.1±3.3[1)2)] |
| Canicular-day application | 46 | 71.8±11.7 | 79.1±5.4[1)3)] | 65.3±6.5 | 83.2±3.5[1)3)] |
| Enteral nutrition | 46 | 72.1±11.3 | 76.3±6.2[1)] | 65.2±6.8 | 78.6±4.1[1)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and the enteral nutrition group, 2) $P<0.05$; compared with the enteral nutrition group, 3) $P<0.05$

**Table 5. Comparison of cellular immunity items ( $\bar{x}$ ±s)**

| Group | *n* | Time | $CD3^+$ (%) | $CD4^+$ (%) | $CD4^+/CD8^+$ | $CD8^+$ (%) |
|---|---|---|---|---|---|---|
| Observation | 46 | Pre-treatment | 57.6±4.4 | 29.8±2.6 | 1.08±0.13 | 30.7±3.1 |
| | | Post-treatment | 69.1±6.5[1)2)] | 40.4±3.9[1)2)] | 1.88±0.27[1)2)] | 20.2±1.4[1)2)] |
| Canicular-day application | 46 | Pre-treatment | 57.4±3.5 | 30.1±2.2 | 1.07±0.11 | 30.5±2.6 |
| | | Post-treatment | 59.6±4.8[1)] | 31.7±2.8[1)] | 1.11±0.14[1)] | 29.3±2.4[1)] |
| Enteral nutrition | 46 | Pre-treatment | 57.2±4.1 | 30.3±2.1 | 1.06±0.14 | 30.2±1.6 |
| | | Post-treatment | 58.6±3.8[1)] | 31.1±2.2[1)] | 1.13±0.15[1)] | 28.6±1.3[1)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and the enteral nutrition group, 2) $P<0.05$

 

**Table 6. Comparison of the blood biochemical items ( $\bar{x}$ ±$s$)**

| Group | $n$ | Time | Hb (g/dL) | TP (g/L) | ALB (g/L) |
|---|---|---|---|---|---|
| Observation | 46 | Pre-treatment | 93.5±1.8 | 47.6±1.3 | 28.4±2.3 |
| | | Post-treatment | 131.4±2.2[1)2)] | 63.5±2.4[1)2)] | 38.9±2.8[1)2)] |
| Canicular-day application | 46 | Pre-treatment | 93.4±1.6 | 47.8±2.1 | 28.1±2.1 |
| | | Post-treatment | 118.5±5.6[1)] | 50.2±2.8[1)] | 30.5±1.7[1)] |
| Enteral nutrition | 46 | Pre-treatment | 93.7±4.7 | 47.5±2.1 | 28.6±2.2 |
| | | Post-treatment | 121.6±3.8[1)3)] | 56.2±2.2[1)3)] | 32.4±2.3[1)3)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and enteral nutrition group, 2) $P<0.05$; compared with the canicular-day application group, 3) $P<0.05$

**Table 7. Comparison of ECP, LPO, and LT ( $\bar{x}$ ±$s$)**

| Group | $n$ | Time | ECP (pg/L) | LPO (nmol/L) | LT (pg/mL) |
|---|---|---|---|---|---|
| Observation | 46 | Pre-treatment | 20.4±4.1 | 18.6±4.1 | 24.8±5.6 |
| | | Post-treatment | 5.7±0.6[1)2)] | 6.5±0.1[1)2)] | 11.2±2.5[1)2)] |
| Canicuar-day application | 46 | Pre-treatment | 20.3±3.7 | 18.7±3.9 | 24.2±5.3 |
| | | Post-treatment | 18.2±2.3[1)3)] | 13.5±1.5[1)3)] | 20.1±4.6[1)3)] |
| Enteral nutrition | 46 | Pre-treatment | 20.5±3.7 | 18.4±4.3 | 24.7±5.8 |
| | | Post-treatment | 19.4±2.1[1)] | 17.3±2.1[1)] | 22.8±4.9[1)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and the enteral nutrition group, 2) $P<0.05$; compared with the enteral nutrition group, 3) $P<0.05$

**Table 8. Comparison of body test results ( $\bar{x}$ ±$s$)**

| Group | $n$ | Time | BW (kg) | TSF (mm) | AMC (cm) |
|---|---|---|---|---|---|
| Observation | 46 | Pre-treatment | 56.2±16.2 | 8.5±2.3 | 20.7±4.5 |
| | | Post-treatment | 63.5±12.8[1)2)] | 9.9±3.1[1)2)] | 29.8±3.5[1)2)] |
| Canicular-day application | 46 | Pre-treatment | 56.8±15.7 | 8.1±2.5 | 20.5±3.9 |
| | | Post-treatment | 57.1±10.3[1)] | 8.7±2.6[1)] | 22.3±3.2[1)] |
| Enteral nutrition | 46 | Pre-treatment | 56.7±15.9 | 8.8±1.8 | 20.8±4.2 |
| | | Post-treatment | 60.4±13.1[1)3)] | 9.2±2.3[1)3)] | 25.4±3.1[1)3)] |

Note: Intra-group comparison, 1) $P<0.05$; compared with the canicular-day application group and the enteral nutrition group, 2) $P<0.05$; compared with the canicular-day application group, 3) $P<0.05$

## 4 Discussion

Children's CVA is a special type of asthma with chronic cough as the major or only symptom, usually aggravated by cold air, dust, or stimulating substances. Due to its untypical symptom, CVA is often misdiagnosed in clinic. If not treated properly, CVA may develop into refractory typical asthma. It's found that the pathogenesis of CVA is related to respiratory inflammatory, neural receptor, allergy, and genetic factor, which is very similar to that of bronchial asthma[7]. Multiple inflammatory cells and transmitters are involved in the respiratory inflammation. $CD3^+$, $CD4^+$, and $CD8^+$ are important participants in the development of CVA, and can be taken as the markers of respiratory reactions[8]. As another major role in inflammatory transmitters, LT can change the vascular permeability and activate the production of mucus by contracting the smooth muscles of bronchus, and assemble eosinophile granulocytes, consequently aggravating the respiratory inflammation[9]. ECP is involved in allergy reactions, always presenting a comparatively high level in patients with bronchial asthma, and it's closely related to the development of CVA[10]. LPO has a certain significance in evaluating the disease condition and severity, and it indicates that CVA patients are under a crossing oxidative stress[11].

Traditional Chinese medicine (TCM) holds that CVA is caused by the dysfunction of the lung, spleen, and kidney, as well as contraction of wind and reverse flow of lung qi. Therefore, CVA should be treated with tonifying the lung, spleen, and kidney as the major

approach, to reinforce the sufficient and reduce the excessive, and enhance the immunity. In this study, Dazhui (GV 14), Dingchuan (EX-B 1), Jingbailao (EX-HN 15), Feishu (BL 13), Shenshu (BL 23), Gaohuang (BL 43), and Pishu (BL 20) were selected for the application treatment, to expel pathogens and resolve phlegm, and ventilate the lung and cease cough[12-15]. Application in canicular days is a unique treatment in TCM, guided by the theories that to treat cold diseases in summer and to treat disease before it arises. Canicular-day application with medications warm and pungent in nature at local points can drive away cold, unblock meridians and collaterals, and supplement healthy qi. In the canicular days, yang qi approaches the highest level; correspondingly, during this period of time, yang qi is also in the most sufficient stage and the metabolism is very active in human body. It makes the medication easily pass through the acupoints and work directly on the affected area. Meanwhile, the warm and pungent medications can raise up skin temperature, dilate vessels, and promote local blood flow. Thus, the medications, acupoints, and meridians work together to regulate the qi and blood, expel pathogens, and strengthen the defensive qi of the body[16-18].

In children's CVA, the consumption of energy and gastrointestinal disorders can lead to malnutrition, and the insufficiency of nutrition will in turn aggravate the dysfunction of the body, making the cough more difficult to control and forming up a vicious cycle[19]. Malnutrition directly reduces the function of respiratory muscles and diaphragm, damages immune function, and may even cause failure of respiration and multiple complications[20]. Rational use of enteral nutrition can promote the production of protein and inhibit its decomposition, improve potential or existent malnutrition state, supply energy and nutrient substrate to the cellular metabolism, correct metabolic disorders, regulate immune function, and promote the recovery. Our study found that canicular-day application plus enteral nutrition can produce a higher clinical efficacy, and more significant effects in improving the symptom score, pulmonary function, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, $CD8^+$, Hb, TP, ALB, ECP, LPO, LT, BW, TSF, and AMC, compared to the separate use of the two methods. It indicates that combination of canicular-day application and enteral nutrition can effectively improve the pulmonary function and symptoms, regulate cellular immune system, improve nutrient state, and enhance the therapeutic efficacy. The results also showed that dry canicular-day application worked better in improving PEF, FEV1, ECP, LPO, and LT compared to enteral nutrition, which is possibly because that canicular-day application can expel phlegm, ventilate the lung and stop cough, dilate vessels, and increase blood flow. However, enteral nutrition showed its advantage in improving the BW, TSF, AMC, Hb, TP, and ALB compared to canicular-day application, which is plausibly due to that enteral nutrition can inhibit the decomposition of protein, supply cellular metabolism with essential energy and nutrient substrate, and regulate metabolism. More details are required to reveal by further studies.

**Conflict of Interest**

The authors declared that there was no potential conflict of interest in this article.

**Acknowledgments**

This work was supported by the Project of Taihe Hospital of Shiyan City (十堰市太和医院院级课题, No. 2014KF21).

**Statement of Informed Consent**

Informed consent was obtained from the guardians of the recruited children in this study.

Received: 6 January 2016/Accepted: 16 February 2016

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**Translator**: Hong Jue (洪珏)