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Magnesium Valproic acid assisted with Compound Danshen Dripping pills repairs abnormal perfusion foci in children with epilepsy

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Abstract

Objective: To explore the repairing effect of Compound Danshen Dripping Pills with magnesium valproate sustained-release tablets on abnormal perfusion foci in epileptic children. Methods: After epileptic onset was controlled, abnormal perfusion foci in children were repaired using Compound Danshen Dripping Pills. The effectiveness of the treatment was evaluated with interictal SPECT, long-term video-EEG, and CT/MRI. Therapeutic drug monitoring was performed before and after treatment. Results: There were 79 boys and 31 girls. Generalized epilepsy was found in 62 cases and focal epilepsy in 48. Epileptic seizures were controlled for an average of 30.2 months. SPECT abnormalities were present in 85 cases (77.3%) before treatment with Compound Danshen Dripping Pills and significantly reduced to 39 cases (35.5%) afterward ($P = 0.00$). The number of abnormal perfusion foci decreased from 129 before treatment to 56 afterward. Conclusions: Compound Danshen Dripping Pills combined with magnesium valproate is an ideal treatment strategy for epilepsy in children because of the high degree to which abnormal perfusion foci are restored to normal.

Keywords

Children with Epilepsy, Compound Danshen Dripping Pills, Magnesium Valproate, Repair, Abnormal Perfusion Foci, Interictal SPECT, Long-Term Video-EEG

1. Introduction

The World Health Organization is determined to conquer epilepsy in the 21st century. Children account for the greatest number of epilepsy cases, and ≤ 80% of child epilepsy can be controlled or cured by medical treatments. Neuroimaging in epilepsy focuses on the correlation of neural networks with dynamic phenomena and clinics [1]. Epilepsy is characterized by clinical onset, epileptiform discharge, and abnormal perfusion foci/metabolic foci as detected by single photon emission computed tomography (SPECT)/positron emission computed tomography (PET). Epileptic seizure and epileptiform discharge are detected through electroencephalogram (EEG), while abnormal perfusion foci/metabolic foci are the pacemaker of epilepsy. The brain is composed of complex neural circuits [2]. Interictal SPECT and PET imaging display hypoperfusion and low metabolic foci (≤ 80%), and ictal SPECT and PET imaging displays hypertransfusion and high metabolic foci (100%), which are used for locating epileptic foci, proposing treatment, and assessing prognosis. SPECT is more sensitive than EEG, *computed tomography* (CT), or MRI [3]. Devous detected 23 abnormal foci via SPECT, 10 of which were not found by MRI scans. Functional SPECT has opened up avenues for therapeutic strategies in the treatment of brain diseases [4].

Abnormalities in brain networks are closely linked with the pathophysiological mechanism of epilepsy, abnormal perfusion, metabolic foci, and clinical seizures. Two generally accepted aspects of abnormal perfusion foci in

epilepsy are: (1) Engle proposed that the occurrence of hypoperfusion foci is partially mediated by the inhibition of healthy neurons or a decrease of neural activity, which are reversible; (2) hypoperfusion foci are located around the lesion, reflecting epileptogenic processes that are closely linked with abnormally functioning regions. Changes in cerebral blood flow directly reflect neural network function in epilepsy [5]. Temporal lobe hypoperfusion is the indicator of early temporal epilepsy [6].

The efficacy of antiepileptic drugs has not improved greatly within the last 40 years [7]. If abnormal perfusion foci in patients with epilepsy are not repaired, abnormal foci in the brain may produce lasting changes. Hypoperfusion foci can induce clinical seizures [8], cause brain dysfunction, and exacerbate epileptic foci [9]. Long-term epileptic seizures result in cerebral ischemia and brain injury, develop into structural lesions, and affect brain development and maturation [10]. Brain lesions cause local cerebral atrophy [11] and induce chronic or refractory epilepsy.

Wang et al previously reported dynamic changes in abnormal perfusion foci in patients with epilepsy after traditional Chinese medicine assisted with antiepileptic drugs. Results showed that perfusion abnormalities in epilepsy could be repaired, and that abnormal perfusion with metabolic foci and biphasic patterns is the third characteristic of human epilepsy seizures [12]. There is the first attempt to introduce traditional Chinese medicine for repairing abnormal perfusion foci in combination with antiepileptic drug treatment [12-18]. Although a single antiepileptic drug can control clinical seizures, other aspects of epilepsy such as the pathophysiological changes, cerebral blood flow, cerebral metabolism, and the epileptic neural network caused by epileptic discharge have yet to be solved. Repairing abnormal foci in epilepsy is also the focus of integrated medicine. This study aims to explore the degree to which Compound Danshen Dripping Pills combined with magnesium valproate can repair abnormal foci in children with epilepsy.

2. Methods

2.1. Participants

Children with epilepsy were recruited from the Epilepsy Centre, No. 2 Hospital of Lanzhou University, China between January 2009 and June 2012. All patients were diagnosed according to the Diagnostic Criteria and Classification formulated by the International League Against Epilepsy in 2001. Inclusion criteria: (1) aged ≤ 12 years, (2) generalized and focal seizures, (3) related EEG (diffused abnormality in EEG and GE, local abnormality in PE (focal), and idiopathic EEG), (4) a history of epileptogenic disease, and (5) abnormal structure revealed by imaging. Exclusion criterion: a continuous epileptic state. Patients who met all criteria were informed of the treatment strategy before experimentation and gave their written consent. Experimental proposals were approved by the Ethics Committee of the Hospital.

One-hundred and ten children (79 boys, 31 girls; mean age: 7.85 years; range: 3–12 years) with epilepsy who were receiving long-term antiepileptic drugs were included in the study. Their conditions were checked by Interictal SPECT, long-term EEG monitoring, and CT/MRI. The concentration of antiepileptic drugs was also monitored before and after treatment. Time since diagnosis was 3 months to 10 years (mean 4.6 years). Among them, 59 cases showed clear etiological factors (12 cases, traumatic brain injury; 14 cases, perinatal injury; 15 cases, febrile convulsion; 4 cases, family history of epilepsy; 1 case, brain infection; 13 cases, multiple etiologies). Generalized epilepsy was found in 62 cases, including 50 cases of generalized tonic-clonic seizures, 4 cases of juvenile myoclonic epilepsy, 3 cases of typical absence seizures, 2 cases of myoclonic seizures, 1 case of myoclonic absence seizures, and 2 cases of myoclonic-astatic seizures. Focal epilepsy was found in 48 cases, including 14 cases of benign epilepsy with centro-temporal spikes and 34 cases of symptomatic focal seizures, 8 cases of simple foci seizures, 4 cases of temporal lobe seizures, and 22 cases of secondary generalized tonic-clonic seizures. In addition, 42 cases (38.1%) of idiopathic epilepsy, 54 cases (49.0%) of symptomatic epilepsy, and 14 cases (12 7%) of cryptogenic epilepsy were also present. Pre-treatment seizure frequency was at most 6 times/year in 40 cases (36.4%), once per month in 50 cases (45.5%), once per week in 18 cases (16.4%), and 3 times/day in 2 cases (1.8%).

2.2. Treatment and Drugs

Drugs: Magnesium valproate sustained-release tablets (State Drug Approval Document Number: h2003057; produced by Xiangzhong Pharmaceutical Co., Ltd., Hunan Province, China; 250 mg/tablet); Compound Danshen Dripping Pills (State Drug Approval Document Number: Z10950111; produced by Tianjin Tasly Pharmaceutical Co., Ltd., Tianjin, China; 27 mg/pill, twice per day). Valproic acid concentration was monitored and ranged from 59.51 ± 17.96 μg. PB, VPA, CBZ, and PHT concentrations were detected with using a Viva-siemens 200 ELISA (LTG, HPLC, Agilent Technologies, type 1100).

Treatment: After the seizure was controlled using magnesium valproate sustained-release tablets, abnormal foci in epileptic children were repaired using Compound Danshen Dripping Pills.

2.3. SPECT Assessment

An E.CAM Single SPECT instrument (Siemens, Chicago, USA) was used for assessment. After patients were intravenously injected with 99mTc-ECD, 30 mCi (Institute of Nuclear Medicine, Jiangyuan Pharmaceutical Factory, Wuxi, China; number: H10980145) for 30 minutes, and cerebral perfusion tomography was performed. Twelve images were used to reconstruct the brain profiles in transection, coronal, and sagittal views. Initial SPECT was

administered 7 days after a recent attack.

Image analysis was performed using semi-quantitative analysis with a mirror ratio (Ra = R/L; R: ROI, regions of interest). Ra refers to the ratio of radiation data uptake at the lesion divided by the radiation data uptake at normal regions (contralateral to the lesion). An Ra ≥ 10% was considered a region of interest (ROI). The measured value of Ra reflects regional cerebral blood flow (rCBF%). The ROI was thus always an abnormal perfusion foci and the non-ROI was calculated using the normal rCBF value. The ratio of radiation data between the ROIs was 8.6 ± 1.2%, ROI hypoperfusion radiation data were 49.4 ± 14.5%, and ROI hypertransfusion radiation was 168.5 ± 23.6%. Hypertransfusion-hypoperfusion refers to two or more concentrated or sparse regions in the brain. The present study showed a hypertransfusion rate of 168% and a hypoperfusion rate of 49%. Pre-treatment EEG and interictal SPECT were performed within 2 days after visiting the first visit to the hospital. Patients were re-checked 12 months after treatment with Compound Danshen Dripping Pills.

Case 1. A 7-year-old boy with epilepsy. Secondary generalized tonic-clonic seizure, normal MRI. No attack after 3 years of Compound Danshen Dripping pills assisted with valproic acid. Before treatment, interictal SPECT displays severe hypoperfusion in the left temporal lobe and part of the left frontal lobe. After treatment, SPECT detects that cerebral perfusion is restored to normal. While epileptiform discharge was found at the left hemisphere before treatment, after treatment the discharges disappeared.

Case 2. A 12-year- girl with epilepsy. Complex partial secondary generalized tonic-clonic seizure,MR shows Beside of the cerebral ventricles showed three abnormal signal. No attacks after 3 years of treatment with Compound Danshen Dripping pills assisted with Magnesium valproic. Before treatment, interictal SPECT shows hypoperfusion at right frontal lobel and temporal lobel. After treatment, interictal SPECT shows that cerebral right frontal lobel and temporal lobel perfusion was restored to normal. While epileptiform discharge was found before treatment, after treatment it had righ temporal lobel discharge.

2.4. Long-Term Video-EEG Assessment

Video-EEG was performed using a Cadwell Easy II (Cadwell, USA). Electrodes were placed according to the international 10-20 standard, and a sphenoid electrode was added to the 43 children who were over six years old. Patients were monitored for 12 hours. EEG analysis and assessment were performed by expert technicians.

2.5. CT/MRI Assessment

A Somatom Sensation 64-slice spiral CT scanner and a Magnetom Sensation 1.5T MRI scanner (Siemens, Germany) were used to collect CT and MRI images. CT-MRI results were analyzed and assessed by technicians.

2.6. Statistical Analysis

Changes in abnormal foci before and after treatment were compared using SPSS 13.0 software (SPSS, Chicago, IL, USA). Variations in long-term EEG were detected using χ^2 test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical Efficacy

Epileptic symptoms were completely controlled in all patients for 12–70 months (mean 30.2 months), with no seizures occurring.

Changes of interictal SPECT and long-term EEG in epileptic children before and after treatment (Tables 1, 2)

Table 1. *Abnormal perfusion foci and perfusion state of interictal SPECT imaging in 110 epileptic children before and after treatment [n (%)]*

	Normal	Abnormal	Hypoperfusion	Hypertransfusion	Hypertransfusion-hypoperfusion	Total abnormal foci
Before treatment	25 (22.7)	85 (77.3)	29 (34.1)	53 (62.4)	3 (3.5)	129
After treatment	71 (64.5)	39 (35.5)	18 (46.2)	20 (51.3)	1 (2.6)	56

3.2. SPECT Imaging before and after Treatment

Before treatment, 85 cases showed abnormalities as detected by SPECT (77.3%), with 129 abnormal perfusion foci. After treatment, SPECT revealed only 39 abnormal cases (35.5%), with 56 abnormal foci. The decrease in SPECT abnormalities was highly statistically significant ($\chi^2 = 39.106$, $P = 0.000$), as was the reduction in abnormal foci.

3.3. Abnormal Foci and Brain Regions

Before treatment, there were 129 abnormal foci in the 110 patients. This included: 42 (32.5%) in the temporal lobe, 40 (31.7%) in the frontal lobe, 22 in the parietal lobe, 5 in the occipital lobe, 4 in the cerebellum, and 12 in other regions. Additionally, 1 was in a large area (involving three brain regions), 1 was in a generalized hypoperfused region, and 2 were in multi-point hypertransfused regions. After treatment, the number of abnormal foci was reduced to 56. This included: 15 in the temporal lobe, 16 in the frontal lobe, 16 in the parietal lobe, 7 in the occipital lobe, 1 in insular lobe, and 1 multi-point punctiform. Temporal lobe repair-rate was 62.3% (27/42) and frontal lobe repair-rate was 60.0% (24/40).

Abnormal foci repair-rate reached 35.2% (19/54) among cases of symptomatic epilepsy, 57.1% (24/42) among cases of idiopathic epilepsy, and 21.4% (3/14) among cases of cryptogenic epilepsy, and differed significantly between

symptomatic and idiopathic epilepsy ($\chi^2 = 6.242$, $P = 0.011$). The repair rate also differed significantly between cases of short (< 3 years) and long (≥ 3 years) disease durations (short: 32.8% (19/58); long: 51.9% (27/52); $P < 0.05$), but did not differ between those who had abnormal and normal CT/MRI (abnormal: 41.2% (7/17); normal: 41.9% (39/93); $\chi^2 = 0.003$, $P = 0.586$).

Table 2. *Comparison of long-term EEG detection in 110 epileptic children before and after treatment [n(%)]*

	Normal	Abnormal	Mildly abnormal	Epileptiform discharge	Local discharge	Generalized discharge
Before treatment	4 (3.6)	106 (96.4)	8 (7.5)	98 (92.5)	28 (28.6)	70 (71.4)
After treatment	64 (58.2)	46 (41.8)	6 (13.0)	40 (87.0)	18 (45.0)	22 (55.0)

3.4. CT-MRI Examination

CT-MRI scans detected 17 abnormal patients (15.5%), including 4 cases of softening foci, 4 cases of temporal atrophy, 2 cases of hippocampal sclerosis, 2 cases of enlarged ventricles, 1 case of heterotopic gray matter, 1 case of abnormal frontal signals, 1 case of cerebral dysplasia, 1 case with hippocampal cysts, and 1 case with septum pellucidum cysts.

Table 3. *Comparison of SPECT and EEG indexes in epileptic children between the abnormal foci-repair group and an anti-epileptic drug group* [n, %]*

Drug	Nature of epilepsy	Number	Time of controlling (month)	SPECT abnormality	Imaging abnormality	Normally increase	Reduced total foci	Reduced discharge
Compound Danshen Dripping Pills group	Children epilepsy	110	32.2	96.4	15.5	41.8	56.6	52.7
Anti-epileptic drugs group	Various epilepsy	77	40.8	93.5	26.2	6.5	19.7	19.5

* The anti-epileptic drug group has been described previously [19].

4. Discussion

Epilepsy in the 110 children was controlled with magnesium valproate (mean duration: 30.2 months) and then patients were treated with Compound Danshen Dripping Pills to repair abnormal perfusion foci. SPECT abnormalities were present in 85 cases (77.3%) before treatment and were reduced to 39 cases (35.5%) after treatment, showing an increase of normal SPECT in 46 cases (41.8%; $P = 0.00$). The number of abnormal perfusion foci was reduced from 129 before treatment to 56 after treatment. Long-term EEG detection results showed abnormalities in 46 cases after treatment, with the number of normal EEG cases increasing by 60 (54.5%, $P = 0.00$). Epileptiform discharges disappeared in 58 cases (52.7%).

The International Treatment Guideline for Epilepsy (2012) gives guidelines that aim to control/reduce epileptic seizures, protect cognition, and improve the quality of life. Valproic acid is a broad-spectrum antiepileptic drug that works via multiple mechanisms, and is effective for generalized and focal seizures. Sustained-release magnesium valproate tablets are more than 20% more effective than conventional tablets [19]. Valproate treatment may bring its effects about through several mechanisms, such as signal-transduction pathways, gene-level changes, increased GABA concentration, glutamate regulation, inhibition of NMDA receptor activation, neuron protection, reduction of inflammation, neurotrophics, promotion of nerve regeneration, reduction of glial cell proliferation, and by blocking apoptosis [20]. Furthermore, magnesium ions can prevent and cure epilepsy, block NMDA receptors, inhibit glutamate reuptake, and increase r-aminobutyric acid type B receptors [21]. When seizures are monitored and controlled by certain concentrations of magnesium valproate, individualized treatment can slightly affect cognitive function [15].

Repair of abnormal perfusion focus and network pharmacology of Chinese medicine

Stefan et al proposed a comprehensive treatment concept for modifying initial injury, protecting nerves, anti-epileptic and disease-modifying [22]. The complex mechanism associated with epilepsy in children determines the appropriate series of treatments. The endogenous anticonvulsant system in epileptic children is defective .. Commonly used antiepileptic drugs may ignore the nerve-endocrine-immune network system [23], which can be well regulated by traditional Chinese medicine. Recently a novel pattern for disease-drug intervention has emerged, involving disease, characterization, genes, targets, and drugs [24]. Thus functional genomics, proteomics, systems biology, and network pharmacology for modern Chinese and Western pharmaceutical sciences can be used in treatment of epilepsy. This provides philosophical evidence for explaining and developing the complexity of life network, disease network, and traditional Chinese medicine network, and realizes the revolutionary changes from "single-gene, single-target, single-drug" to “multi-target, multi-channel” [25]. Modern medicine previously focused on the decomposition and modern network pharmacology changes [26]. A single Chinese drug can act on multiple targets, and a variety of traditional Chinese medicine function on the same target. A crucial principle of traditional Chinese medical treatment of epilepsy is to activate blood circulation and

dissipate blood stasis. Some Traditional herbs (Radix Salviae Miltiorrhizae, Safflower, Rhizoma Chuanxiong, Herba Erigerontis, Semen Persicae, Radix Notoginseng, and Triumfetta) contain 322 chemical components, which correspond to 218 targets in 61 reaction pathways. Thus, philosophically guided medical treatment that integrates traditional Chinese and western medicine is the ideal option for children with epilepsy. Repairing abnormal perfusion foci is a breakthrough in the treatment of epilepsy.

The mechanism of action of Compound Danshen Dripping Pills

Compound Danshen Dripping Pills are the first modern traditional Chinese medicine introduced to phase III clinical trials by the Federal Drug Administration in the United States. They are composed of Radix Salviae Miltiorrhizae, Radix Notoginseng, and Broneolum Syntheticum, which play a synergic role on multiple targets, thus maximizing therapeutic effect. Compound Danshen Dripping Pills combined with magnesium valproate tablets is a new emerging treatment of epilepsy in children that induces a high repair rate, protects neurons, and results in fewer reperfusion injuries. Compound Danshen Dripping Pills have a variety of functions. First, Radix Salviae Miltiorrhizae alleviates monoamine neurotransmitter and neuropeptide disorders in cerebral ischemia, partially down-regulates the expression of immediate early genes (c-fos gene), reduces epileptiform discharges, and inhibits epileptic seizures. Second, it suppresses abnormal elevation of B-endorphins, reduces brain damage, repairs brain tissue, and improves convulsion thresholds. Third, it protects against cerebral ischemia-reperfusion injury through multiple links, stabilizes the membrane and antagonizes calcium ions, reduces excitotoxicity of excitatory amino acids and anti-free radicals, and attenuates cerebral edema [27] better than nimodipine[28] . Fourth, it significantly improves learning and memory impairment in mice and effectively treats mouse models of long-term mental disorders [29]. Fifth, Total Saponins of Panax Notoginseng reduces apoptosis and necrosis, inhibits Caspase-3 expression after cerebral ischemia-reperfusion, and promotes neuronal survival [30]. Last, Broneolum Syntheticum promotes the safe opening of the blood-brain barrier (does not cause pathological damage), and increases the concentration of antiepileptic drugs in the brain [31].

The restoration of abnormal foci in the present study is characterized by the following features

(1) The rate at which abnormal perfusion foci in children with epilepsy were repaired was significantly higher than that in adults

After treatment, the number of cases with normal SPECT increased by 46 (41.8%), and the number of abnormal foci decreased by 56.6%, which was significantly better than when epilepsy was treated with simple AEDs (normal SPECT increased by 6.5%; abnormal foci decreased by 19.7%) [18]. Decrease in convulsion threshold, brain damage, and predisposing factors are the three leading causes of epilepsy. These factors are prevalent in children because of endogenous antiepileptic system defects and incomplete nerve-endocrine-immune networks. Brain damage may affect degenerative epileptic foci and surrounding hypoperfusion zones, increase endothelin synthesis and release into peripheral tissue, lead to abnormal elevation of cerebral microvascular spasm-cerebral ischemia-excitatory amino acids and epileptiform discharges [32]. Compound Danshen Dripping Pills inhibit abnormal elevation of excitatory amino acids after ischemia, reduce epileptiform discharges, and attenuate brain edema. Valproate prevents neurodegeneration and the formation of neuronal fiber tangles and potential neuroprotection, and prevents the transformation from dynamic abnormal perfusion foci to static brain structural abnormalities, which may explain the increased repair rate in epileptic children. In comparison with a carbamazepine group, normal cases increased by 24% and abnormal foci decreased by 34.3%, which was significantly lower than the repair rate in a valproate group [33].

(2) The nature of epilepsy and seizure type are the keys to the repair rate of abnormal perfusion foci

Idiopathic epilepsy and benign rolandic epilepsy had significantly higher repair rates than symptomatic epilepsy, focal epilepsy, or secondarily generalized seizures (idiopathic epilepsy: 48%; benign childhood epilepsy: 67% [16, 34]). While in temporal epilepsy with brain-structure abnormalities, normal foci were shown to increase by 4.5% [35], in this study the repair rate of abnormal foci accompanied with abnormal or normal radiographic images was 41%. This evidence suggests that some abnormal foci that did not show up with normal radiological tests were located at the process of degeneration. The repair rate in focal epilepsy has been reported to be 12.0% [12], which is often accompanied by radiographic abnormalities and sub-structural abnormalities. The repair rate of abnormal foci in cases of idiopathic, high perfusion, no etiology, and normal radiology was significantly higher than that in cases of systematic, low perfusion, clear cause, and abnormal radiography [36].

(3) Correlation of reparative Chinese herbal medicine and antiepileptic drugs with abnormal perfusion foci

Because epileptic brain injury can result from neuro-excitotoxicity that follows repeated seizures and subsequent excitatory chain reactions, anti-epileptic therapy can effectively prevent brain damage. In contrast to adults, the brains of children are still developing, and epileptic brain damage may seriously impact their brains. Repairing abnormal foci in the brain is a very complex pathophysiological process. Magnesium valproate is an effective neuroprotective agent and repair agent, and we tentatively infer that Compound Danshen Dripping Pills combined with magnesium valproate is an ideal therapeutic option for treating epilepsy in children.

(4) Correlation of the etiological factor and the disease duration with the repair of abnormal perfusion foci.

Epilepsy shows different etiological factors and disease durations between children and adults. The duration in some children with epilepsy is shorter than the formation time of abnormal foci in adults, for example generalized tonic-clonic seizure in children versus temporal epilepsy in adults). In the present study, the rate at which abnormal perfusion foci were repaired showed significantly differed ($P < 0.05$) between those with short (32.8%) and long (51.9%) disease durations. One interpretation of this result is that the longer the treatment lasts, the higher the repair rate is. This finding provides a schedule controlled by physicians. Unlike the general time limit for withdrawal (3–5 years), repairing abnormal foci may reduce the recurrence of epilepsy in some cases. The results of the present study showed that the repair rate of abnormal perfusion foci was 35.2% in symptomatic epilepsy, 57.1% in idiopathic epilepsy, and 21.4% in cryptogenic epilepsy. The repair rate in symptomatic epilepsy and cryptogenic epilepsy was lower than that of idiopathic epilepsy, likely because lesions of unknown origin occur in the former two epilepsies that cannot be detected by structural imaging.

(5) Correlation of repairing abnormal perfusion foci with eliminating epileptiform discharges.

EEG abnormalities were found in 96.4% of cases and 92.5% presented discharges before treatment. After treatment, the number of cases with EEG abnormalities was reduced to 46 cases, while the number of cases with normal EEG was increased by 60 (54.5%, $P = 0.000$). Discharge disappeared in 58 cases (52.7%). Valproate is a kind of broad-spectrum GABA agonist, and after treatment, the number of normal cases increased and epileptiform discharges disappeared. Furthermore, the number of cases with normal EEG continued increasing as the treatment continued. After treatment, both focal and generalized epileptiform discharges showed similar improvements in the number of repaired abnormal perfusion foci (50% and 45.5%, respectively) [33], and valproate treatment has been shown to give similar results as carbamazepine in treatment for some kinds of epilepsy [37]. In this study, 48 cases with focal epilepsy (43.6%) were completely controlled. In addition, epileptiform discharges disappeared in 52.7% cases as assessed by EEG for 12 hours. Long-duration EEG is a necessary tool for detecting the disappearance of epileptiform discharges (although, unfortunately it is still ineffective in some deep brain regions). The presence of epileptiform discharges indicates the continuous existence of abnormal foci and deserves long-term treatment.

5 Conclusion

The traditional Chinese medicine compound danshen dropping pill and valproic acid magnesium a variety of mechanisms joint control seizures, The repair mechanisms of traditional Chinese medicine (TCM) is synergistic effect of traditional Chinese medicine network pharmacology. Repair of abnormal perfusion foci of children with epilepsy and normal high of increase rate and abnormal perfusion foci reduced to 56.6% and Is the ideal of the combined treatment of epilepsy in children.

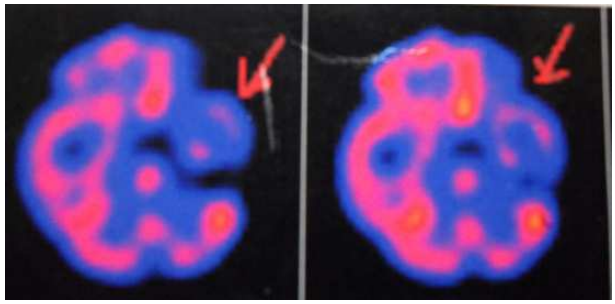

Figure 1. A,B.*SPECT before treatment: Severe hypoperfusion in the left temporal lobe (A) and frontal lobe.*

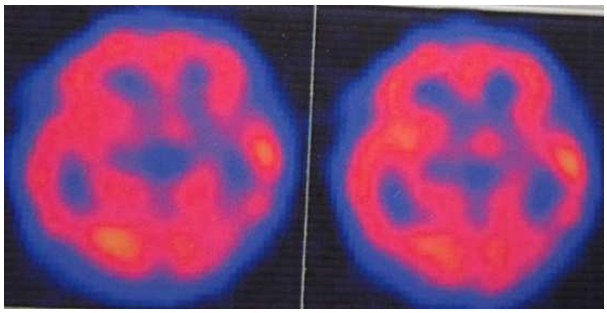

Figure 2. *A, B SPECT after treatment: Cerebral perfusion restored to normal.*

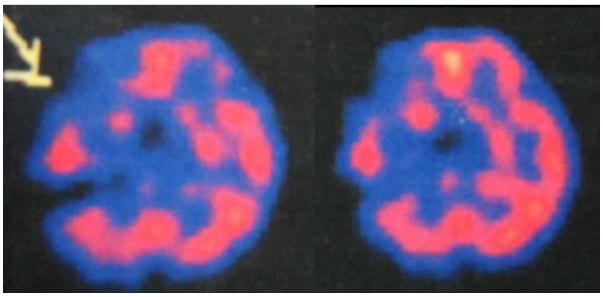

Figure 3. *A, B SPECT before treatment: Hypoperfusion at frontal and temporal lobel.*

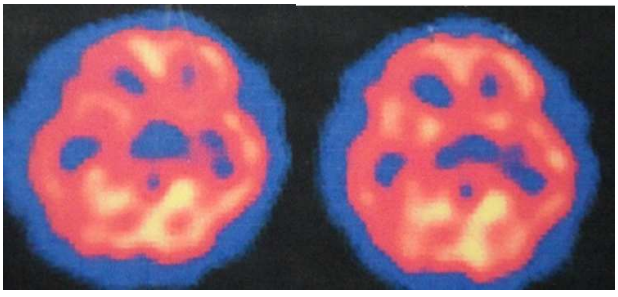

Figure 4. *A, B After treatment, interictal SPECT shows that cerebral perfusion was restored to normal*

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