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# Observation on the efficacy of Xiao Chai Hu Tang plus minus Tang combined with sodium valproate in the treatment of meningitis-associated epilepsy

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**Abstract**: Meningitis is a neurological condition that can be severe causing epilepsy. This study analyzed the efficacy of Xiao Chai Hu Tang plus minus Tang combined with sodium valproate in the treatment of meningitis-associated epilepsy. 100 patients with meningitis-associated epilepsy during June 2022 to June 2024 were randomised to control group ($n$=50) and study group ($n$=50). Both groups were treated with sodium valproate and study group was added Xiao Chai Hu Tang plus minus Tang treatment. To evaluate the traditional Chinese medicine symptom (TCMS) scores, cerebrospinal fluid returning to normal proportion, neurological factors, inflammatory factors, immune indicators, life qualities scores, functional area scores, clinical efficacy and adverse reactions incidence in both groups. All the results of the both groups post-therapy were better versus pre-therapy. Post-therapy, the TCMS scores, erebrospinal fluid returning to normal proportion, neurological factors, immune indicators, life qualities scores, functional area scores and clinical efficacy were above to control group, the inflammatory factors and adverse reactions incidence were below in study group ($p$<0.05). The efficacy of this combination therapy for the treatment of meningitis-associated epilepsy is accurate and has high clinical value.

**Keywords**: Xiao Chai Hu Tang plus minus Tang; sodium valproate; meningitis; epilepsy; inflammatory factor

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## INTRODUCTION

Meningitis being the infectious diseases of the centre of nerve systems caused by a variety of viruses, which is a serious and common brain disease in clinical practice (Wasserman *et al*., 2025). The pathogenesis of this disease is still unclear and it is generally believed that it may be related to viral infections and the immune response caused by the virus, which triggers diffuse inflammation of the soft meninges, resulting in the meninges, brain metabolism and central nervous system dysfunction (Kohil *et al*., 2021). Its main clinical manifestations are fever, headache and meningeal irritation and patients also have hearing impairment, memory loss, mobility disorders and even epileptic seizures, cardiopulmonary and renal failure, shock and other conditions, which seriously affects the patient's life safety and if the treatment is not timely, the treatment is inappropriate and the course of the disease does not heal, then it can further lead to acute brain injury resulting in a poor prognosis, which will lead to a higher fatality rate and disability rate (Bystritsky and Chow, 2022; H Liu *et al*., 2025). Epilepsy is a neurological syndrome caused by abnormal discharges in the brain (Ramantani *et al*., 2025). It being a commonly occurring neurosis that can occur with seizures at any age, transient and repetitive symptoms and is often accompanied by behavioural and autonomic dysfunction, which has a great impact on the health, life and family and reduces the qualities of life (Anwar *et al*., 2020). General diagnosis of epilepsy mainly takes the electroencephalogram and neuroimaging, if abnormal discharge foci are found, timely and effective treatment is needed, in which the initial drug selection is very important, the first choice of broad-spectrum antiepileptic drug therapy, such as sodium valproate is widely used, with the advantages of fast absorption and good efficacy on generalised seizures, but the coverage of the type of a single drug is not comprehensive enough and there are still some patients with epileptic seizures that are not well controlled. Therefore, the combination of other drugs is needed (S He *et al*., 2025; Thijs *et al*., 2019). After meningitis triggers epilepsy, the condition becomes more complicated, affecting the therapeutic effect and clinical prognosis and patients are often accompanied by neuropsychiatric disorders, impaired psychosocial functioning and a sense of shame, with a significant decline in the quality of life. (Ramantani and Holthausen, 2017).

In Chinese medicine, meningitis-associated epilepsy belongs to the categories of 'epilepsy', 'spasm' and 'warm disease'. Chinese medicine has a long history of treating

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such diseases and a relatively complete theoretical system has been formed in the Qing Dynasty. The disease changes rapidly, the disease is more directly into the qi, manifested as strong heat, sweat, thirst and pulse flooding and other qi heat evidence (P Wang *et al*., 2024). In the course of the disease, rainwater and dampness can be seen in the chest plague, dullness, heavy body, etc., exhaustion of qi and injury to the fluid and the external release of fluid, the evil into the heart camp and blood, leading to liver wind within the movement and the occurrence of fainting, blood and other critical illnesses, the above symptoms can be gradually recovered through active treatment, if the disease is prolonged, severe, improper treatment can be left with paralysis, aphasia, aphasia, or death (Wu *et al*., 2023). Xiao Chai Hu Tang is a classic formula in Chinese medicine for treating this type of disease, in which Chaihu has the effect of dispersing the liver and resolving depression, regulating Ying and Wei. Radix Rehmanniae Praeparata has the effect of clearing heat and cooling blood, nourishing Yin and nourishing blood. Zixue San and Baifang Zhi Bao San are mainly used in viral encephalitis with heat poison and phlegm directly entering the heart, high fever and convulsion, delirium and other acute and critical diseases. Codonopsis helps strengthen the liver and spleen, nourish the blood and generates fluids. Qing Hanxia dries dampness and resolves phlegm, reduces rebelliousness, stops vomiting, eliminates lumps and disperses knots. Acacia solves depression and calms the mind. Lily nourishes Yin, moistening the lung, clearing the heart and calming the mind. The jujube nourishes the spleen and stomach, benefiting the vital energy and generating fluids. Ginger strengthens the spleen, nourishes the stomach, warms the body, stops vomiting, dissolves phlegm and relieves cough. Scutellaria baicalensis clears fire from the heart and relieves irritability. Radix et Rhizoma Glycyrrhizae can harmonise all the medicines and moderate the medicinal properties. The combination of all medicines has the effect of dispersing the liver and regulating qi, harmonising the stomach and strengthening the spleen and clearing heat and removing toxins. It can regulate the balance of yin and yang in body and regulate the operation of temper and blood, which can effectively improve the patient's physical condition and have a long-lasting effect (Ting *et al*., 2020; J Wang *et al*., 2023).

The research reports the treatment of this condition, the use of heat-clearing and toxin-dissolving medicines promotes the absorption of inflammation, prevents heart-yang deficiency and detoxifies the liver and Xiao Chai Hu Tang of traditional Chinese medicine has been found to be highly effective in this regard (Mingyu *et al*., 2003). In recent years, the combination of Chinese and Western medicine has achieved good therapeutic results in a variety of inflammatory diseases, Zheng (2018) reported on a study on the treatment of paediatric septic meningitis with Yin Qiao San addition and subtraction combined with cefotaxime sodium found that the combination of Chinese and Western medicines was effective in improving the clinical symptoms of the patients. Some studies have reported that the combination of Chinese and Western medicines reduces the monthly seizure frequency and EEG abnormalities in patients with epilepsy, improves seizure control and thus reduces the risk of adverse events (Zhao *et al*., 2022). It can be seen that the combined treatment of Chinese and Western medicine can effectively improve the clinical efficacy of patients with meningitis or epilepsy.

Currently, meningitis-associated epilepsy symptoms pose a greater challenge to clinical treatment and, studies of the Chinese medicine Xiao Chai Hu Tang combined with Western medicine to treat this condition have not been reported. In this context, we used Xiao Chai Hu Tang plus minus Tang combined with sodium valproate to treat meningitis-associated epilepsy in order to provide a new reference therapy for its clinical treatment.

## MATERIALS AND METHODS

### *Criteria for selection*

*Diagnostic standards*

(1) Chinese medicine diagnostic criteria were consistent with reference to the Diagnostic Criteria for Disease Evidence in Traditional Chinese Medicine (Li *et al*., 2023) and the Clinical Diagnostic and Treatment Guidelines-Epilepsy Subchapter of the Chinese Medical Association (Xu *et al*., 2024). (2) Western medical diagnostic criteria refer to the diagnostic criteria related to meningitis-associated epilepsy in the Clinical Diagnostic and Treatment Guidelines-Neurology Subchapter (Z Chen *et al*., 2018; Hall *et al*., 2022).

### *Inclusion criteria*

(1) The above diagnostic criteria were met. (2) Patients were available for postoperative review and follow-up and the clinical data were complete. (3) Patients and their families signed an information protocol, including informed consent for the relevant agents and herbs used during this study.

### *Exclusion criteria*

(1) Patients with combined malignant tumours and severe organ insufficiency. (2) Patients with other types of infectious diseases. (3) Patients with histories of allergies or contraindications to the medications employed in the study, such as peptic ulcers. (4) Patients who have undergone surgical procedures in the last month or have active bleeding, shock and so on. (5) Others who are not eligible for the study.

### *General informations*

One hundred patients with meningitis-associated epilepsy received during June 2022 to June 2024 were categorised to two groups of 50 patients each depending on the different treatment protocols. Control group: 23 females, 27 males, age 51~70 years old, mean age 60.08±4.16 years

old, disease duration 3-20 months, mean 10.94±0.39 months. Study group: 26 females and 24 males, age 51-70 years old, mean age 59.65±2.74 years old, disease duration 3-20 months, mean 11.16±0.65 months.

The study research followed the Declaration of Helsinki, all participants signed an informed consent form and the privacy and rights of all patients were strictly protected. The research was reviewed and endorsed by Chinese PLA General Hospital's ethical committees.

***Randomisation and blinding***

A total of 100 patients with meningitis-associated epilepsy were enrolled in the clinical diagnostic trial and assigned to the observation and control groups according to a computer programme-generated random allocation table. Randomisation was carried out by an independent member of staff to minimise the risk of allocation concealment. The specific task was to place each allocation in a separate envelope, a process that was opaque to participants. While the intervention could not be blinded to patients and treating physicians, the study outcome assessor was blinded to treatment allocation.

***Treatment***

Patients in both groups were treated with antiviral, anti-inflammatory, cranial pressure-lowering and vasodilating therapies, etc. (J Wang *et al*., 2024). For patients with febrile symptoms, adopt physical or pharmacological cooling to ensure that the body temperature is controlled within a safe range. Adjust the water-electrolyte balance of patients through intravenous infusion or oral rehydration to prevent dehydration or electrolyte disorders. For patients with increased intracranial pressure, use mannitol injection (Drug code: H13023037, specification: 250 mL/g, Shijiazhuang Four Drugs Co., Ltd. Usage dosage: 1~2 g/kg according to body weight or 30~60 g/m$^2$ according to body surface area, in 15%~20% concentration solution in 30~60 min for intravenous drip. The dose is reduced to 0.5 g/kg when the patient is debilitated.) and other drugs to effectively reduce intracranial pressure and reduce cerebral oedema. For patients with convulsive symptoms, sedative drugs such as secobarbital sodium capsules (Drug code: H31021356, specification: 0.1 g, Shanghai Hengshan Pharmaceutical Co., Ltd. Usage dosage: 30~50 mg once, 3~4 times daily) are given to control convulsive seizures. Meningitis antiviral treatment chooses antiviral drugs such as acyclovir injection (Drug code: H20051749; specification: 10 mL: 0.25 g, Shan Dongfang Ming Pharmaceutical Group Co., Ltd. Usage dosage: 5 mg/kg, 2 times/d.). In order to promote the recovery of brain function, drugs to promote the metabolism of brain cells and neurotrophic drugs can be taken, such as citicoline sodium injection (Drug code: H19999349, specification: 2 mL: 0.1 g; Shaanxi Duns Pharmaceutical Co., Ltd.) and vitamin B complex tablets (Drug code: H50020164, specification: 1000 tablets. Southwest Pharmaceutical Co., Ltd. Usage dosage: 1~3 tablets at a time, 3 times a day).

Patients in the control group were treated with sodium valproate, which was taken orally as 600 mg/times twice a day in the form of sodium valproate tablets (Drug code: H43020873, specification: 100 mg/tablet. Hunan Xiangzhong Pharmaceutical Co., Ltd.). Patients in the study group were granted Xiao Chai Hu Tang Plus Minus Tang treatment based on the control group (C Wang *et al*., 2023). The formula includes Chai Hu 15 g, Codonopsis Pilosulae 15 g, Pinellia Tuber 15 g, Jujube 10 g, Ginger 10 g, Acacia Sinensis 30 g, Lily of the Valley 30 g each, Zi Xue San 9 g, Ju Fang Zhi Bao San 9 g, Radix Rehmanniae Glutinosa 15 g, Milkvetch Root 9 g and Radix Glycyrrhizae Praeparata 6 g. Boil with warm water to make soup, patients with high fever add chrysanthemum 9 g, 1 dose per day, each dose is divided into 2 times. 7 d was one course of treatment and the both groups treated for 6 courses of treatment consecutively.

***Indicators for evaluating efficacy***

*Traditionally Chinese Medicine Symptoms (TCMS) Scores*

The TCMS including headache and yellow tongue were scored in both groups of patients (Tsoupras *et al*., 2019), which could be counted as 0, 1, 2 and 3 depending on the severity of the symptoms and the higher the score, the more severe the symptoms.

***Percentage of cerebrospinal fluid returning to normal within 7 d***

Lumbar puncture was performed again in both groups after the 7 d of treatment and the number of cases of return of cerebrospinal fluid to normal was recorded (Ren *et al*., 2020).

***Neurological factors***

Neurological factors in serum of the both groups of patients were detected (Kheirouri *et al*., 2019), patients' venous blood was extracted, centrifuged at high speed 3500 r/min with a radius of 10 cm for 10 min and the supernatant was taken after serum isolation and serum specimens were detected uniformly by ELISA in the Laboratory Department of our hospital and the patients' postoperative serum neurological factors levels were recorded respectively . The serum levels of BDNF and NGF were analysed by human brain-derived neurotrophic factor (BDNF) ELISA kit (CB12019-Hu, Shanghai Coibo Biotechnology Co., Ltd.) and human nerve growth factor (NGF) ELISA kit (CB11248-Hu, Shanghai Coibo Biotechnology Co., Ltd.), respectively.

***Inflammatory factor***

The inflammatory factors of the patients' serum were detected (Fang *et al*., 2019) and serum contents of IL-6, TNF-α and IL-β were analysed by Human tumor necrosis factor-α (TNF-α) ELISA Kit (97072ES96, Shanghai Yeasen Biotechnology Co., Ltd.)，Human interleukin-6 (IL-6) ELISA Kit (PI330, Beyotime Biotechnology) and Human interleukin-β (IL-β) ELISA Kit (PI305, Beyotime Biotechnology), respectively.

***Immunological function***

The serum levels of immunoglobulins were analysed separately in two groups of patients (M Chen *et al*., 2022), serum specimens were tested by ELISA method uniformly by our laboratory department, using Human Immunoglobulin A (IgA) ELISA Kit (D711189-0096, Shanghai Sangon Biotech Co., Ltd.), Human Immunoglobulin G (IgG) ELISA Kit (D711074-0096, Shanghai Sangon Biotech Co., Ltd.) and Human Immunoglobulin M (IgM) ELISA Kit (ab214568, Abcam Plc) were used to detect IgA, IgG and IgM levels.

***Quality of life scores***

The Activities of Daily Living Scale (DLS) and the Quality of Life Scale-31 (QLS-31) were scored pre- and Post-therapy (Tombini *et al*., 2021), both out of 100 and both with higher scores.

***Functional area scoring***

Cognitive functioning was assessed using the Neuropsychological Developmental Scale (Fuermaier *et al*., 2019), which consists of five functional areas: the gross motor test, the fine motor test, the adaptive skills test, the verbal skills test and the social behaviour test. The patients' functional scores were recorded before treatment and after 6 and 12 months of treatment, respectively, all out of 100, all with higher scores.

***Clinical efficacy***

Referring to the criteria for evaluating the efficacy of epilepsy medications in the AAN/AES practice guidelines (Gidal *et al*., 2024), combining the post-treatment seizures of the two groups of patients was used to assess the clinical efficacy (Talwar *et al*., 2023). Significant effect: complete control of epilepsy disappearance and no abnormal electroencephalogram discharges. Effective: seizure frequency reduction of 50% to 100%, electroencephalographic discharge index reduction of ≥50%. Ineffective: seizure frequency reduction of <50%, epilepsy reduction of <50% and <50% reduction in electroencephalographic discharge index. Overall effective rate = (significant effect + effective)/total cases × 100%.

***Occurrence of adverse events***

The number of patient cases in which diarrhoea, nausea and vomiting, gastrointestinal cramps and headache occurred during the treatment period were counted and the incidence of adverse reactions was analysed (Heckroth *et al*., 2021).

***Sample size calculation***

A power analysis was performed in this study to determine the sample size required to detect a statistically significant difference. The sample size was calculated based on the primary outcome of the TCMS score after treatment. At an alpha level of 0.05 and a power of 90%, the results of the study showed that a sample size of 42 patients per group was required. Therefore, in order to draw reliable conclusions, the sample size for this study was 50 cases per group. This study was conducted using G*Power 3.1.9.7 software.

***Ethical approval***

The research was reviewed and endorsed by Chinese PLA General Hospital's ethical committees. (ky20220507)

## STATISTICAL ANALYSIS

The data collected in this study were analysed using IBM SPSS windows statistical software, version 27.0 (IBMCorp., Armonk, New York, USA) software. Normality of continuous data was assessed using the Kolmonorov-Smirnov test. Continuous categories of experimental data that conformed to a normal distribution were expressed as ( $\bar{x}$±s). Comparisons were made using independent samples *t*-test. Count data were expressed as frequencies or frequencies, comparisons were made using the $x^2$ test and associations between variables were analysed using Pearson's method. The $p<0.05$ was the level of statistical significance.

## RESULTS

***Basic information***

The 100 patients who participated in the study were divided into two groups with comparable baseline characteristics (table 1). These results suggest that the two groups were well matched in terms of baseline characteristics, minimising the risk of confounding variables that might affect the study results.

***TCMS scores***

The results of the comparisons of TCMS scores of both groups are shown in table 2, the TCMS scores of both groups of patients post-therapy were below to pre-therapy and the patients in the study group were significantly below to the control group ($p<0.05$).

***Percentage of cerebrospinal fluid returning to normal within 7 d***

The results of the comparison of the recovery rate of cerebrospinal fluid within 7 d among the both groups are presented in table 3 and the recovery rate in the study group was above to control group, suggesting the time for the recovery of cerebrospinal fluid to normal was remarkably shortened after treatment ($p<0.05$).

***Neurological factors***

The results of the neurological factors analyses of the both groups of patients are demonstrated in table 4 and no significant difference between the two groups of patients in BDNF and NGF pre-therapy ($p>0.05$). Post-therapy, neurological factors improved in both groups and were significantly higher in the study group than in the control group ($p<0.05$).

**Table1**: Baseline characteristics of patients in each group

| Parameter | Control group ($n$=50) | Study group ($n$=50) | $t/x^2$ | $P$ |
|---|---|---|---|---|
| Age (years) | 60.08±4.16 | 59.65±2.74 | -0.416 | 0.678 |
| Gender (Male/Female) | 23/27 | 26/24 | 0.322 | 0.571 |
| Weight (kg) | 61.05±4.92 | 60.83±6.47 | -0.146 | 0.884 |
| Disease duration (month) | 10.94±0.39 | 11.16±0.65 | 0.448 | 0.655 |

**Table 2**: Comparison of platelet aggregation rates ( $\bar{x}$±s, scores)

| norm | time | Control group ($n$=50) | Study group ($n$=50) |
|---|---|---|---|
| Headache | Pre-therapy | 2.74±0.42 | 2.84±0.40 |
| | Post-therapy | 1.91±0.53* | 1.62±0.46*a |
| Yellow tongue | Pre-therapy | 1.01±0.31 | 1.03±0.33 |
| | Post-therapy | 0.69±0.15* | 0.51±0.17*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p$<0.05; 'a' indicates remarkable differences versus control group, $p$<0.05

**Table 3**: Comparisons of the proportion of cerebrospinal fluid returning to normal ( $\bar{x}$±s, %)

| Group ($n$=50) | ≤ 7 d | > 7 d |
|---|---|---|
| Control group | 22 | 28 |
| Study group | 34 | 16 |
| $x^2$ | 5.844 | |
| $P$ | <0.05 | |

Note: '*' indicates remarkable differences versus pre-therapy, $p$<0.05; 'a' indicates remarkable differences versus control group, $p$<0.05

**Table** 4: Comparison of Neurofactors ( $\bar{x}$±s)

| norm | time | Control group ($n$=50) | Study group ($n$=50) |
|---|---|---|---|
| BDNF | Pre-therapy | 120.20±10.76 | 120.03±12.98 |
| (pg/mL) | Post-therapy | 153.68±15.04* | 197.90±16.53*a |
| NGF | Pre-therapy | 489.04±46.19 | 487.96±44.79 |
| (ng/mL) | Post-therapy | 531.78±48.03* | 590.80±49.08*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p$<0.05; 'a' indicates remarkable differences versus control group, $p$<0.05

**Table 5**: Inflammatory factor indicators ( $\bar{x}$±s, %)

| norm | time | Control group ($n$=50) | Study group ($n$=50) |
|---|---|---|---|
| TNF-α | Pre-therapy | 8.08±1.47 | 7.40±1.66 |
| (pg/mL) | Post-therapy | 6.04±1.19* | 4.97±1.34*a |
| IL-6 | Pre-therapy | 83.99±6.07 | 84.30±5.50 |
| (pg/mL) | Post-therapy | 53.40±2.99* | 62.54±3.54*a |
| IL-1β | Pre-therapy | 6.38±1.82 | 6.61±1.76 |
| (pg/mL) | Post-therapy | 4.11±0.80* | 3.32±1.08*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p$<0.05; 'a' indicates remarkable differences versus control group, $p$<0.05

**Table 6**: Comparison of immunoglobulin levels ( $\bar{x}$±s, g/L)

| norm | time | Control group (*n*=50) | Study group (*n*=50) |
|---|---|---|---|
| IgA | Pre-therapy | 3.50±1.04 | 3.42±0.93 |
| | Post-therapy | 2.65±0.26* | 1.99±0.28*a |
| IgG | Pre-therapy | 13.11±2.81 | 13.52±2.84 |
| | Post-therapy | 11.49±2.23* | 9.83±1.95*a |
| IgM | Pre-therapy | 1.28±0.21 | 1.29±0.17 |
| | Post-therapy | 1.09±0.09* | 0.89±0.10*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p<0.05$; 'a' indicates remarkable differences versus control group, $p<0.05$

**Table 7**: QLS-31 ( $\bar{x}$±s, score)

| norm | time | Control group (*n*=50) | Study group (*n*=50) |
|---|---|---|---|
| ADL | Pre-therapy | 46.12±3.60 | 45.71±3.34 |
| | Post-therapy | 65.71±5.58* | 72.13±5.06*a |
| QOLIE-31 | Pre-therapy | 65.83±6.24 | 66.68±5.54 |
| | Post-therapy | 72.41±6.51* | 83.06±8.16*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p<0.05$; 'a' indicates remarkable differences versus control group, $p<0.05$

**Table 8**: Patient functional area scores at different time points ( $\bar{x}$±s, score)

| norm | time | Control group (*n*=50) | Study group (*n*=50) |
|---|---|---|---|
| Grand Motion | Pre-therapy | 59.98±9.53 | 58.66±14.60 |
| | Post-therapy | 66.27±12.82* | 71.66±11.59*a |
| Fine Motor | Pre-therapy | 48.16±10.74 | 49.57±10.56 |
| | Post-therapy | 48.66±11.66* | 64.89±10.31*a |
| Adaptability | Pre-therapy | 51.22±10.28 | 50.44±11.51 |
| | Post-therapy | 56.22±11.01* | 56.73±12.07*a |
| Speech | Pre-therapy | 43.03±13.14 | 45.63±12.26 |
| | Post-therapy | 45.69±10.94* | 50.49±8.25*a |
| Social behaviour | Pre-therapy | 39.62±7.40 | 41.39±9.97 |
| | Post-therapy | 49.78±11.02* | 52.81±10.12*a |

Note: '*' indicates remarkable differences versus pre-therapy, $p<0.05$; 'a' indicates remarkable differences versus control group, $p<0.05$

**Table 9**: Comparison of treatment effects (%)

| Group (*n*=50) | Significant effect | Effective | Ineffective | Overall Effective Rate |
|---|---|---|---|---|
| Control group | 24 | 17 | 9 | 41（82%） |
| Study group | 28 | 20 | 2 | 48（96%） |
| $x^2$ | | | | 10.010 |
| *P* | | | | <0.05 |

**Table 10**: Occurrence of adverse reactions (%)

| Group (*n*=50) | Diarrhoea | Nausea and vomiting | Gastrointestinal cramps | Headache | Total incidence |
|---|---|---|---|---|---|
| Control group | 2 | 1 | 2 | 2 | 8（16%） |
| Study group | 1 | 1 | 0 | 0 | 3（6%） |
| $x^2$ | 0.687 | 0.000 | 4.082 | 4.082 | 5.107 |
| *P* | 0.407 | 1.000 | <0.05 | <0.05 | <0.05 |

***Inflammatory factor***

The results of the analysis of inflammatory factors in the two groups of patients are demonstrated in table 5 and no significant difference in the level of inflammatory factors between the two groups of patients pre-therapy ($p>0.05$). The levels of TNF-α, IL-6 and IL-1β were markedly reduced in both groups post-therapy and the study group were below in control group ($p<0.05$).

***Immune function***

The results of the analysis of the immune function indexes of both groups are demonstrated in table 6, pre-therapy, no significant difference among the IgA, IgG and IgM contents of the both groups of patients ($p<0.05$). Post-therapy, the immunoglobulin content of patients in both groups depressed significantly and the study group was below in the control group ($p<0.05$).

***Comparisons of qualities of life scores***

The results of the daily living activities scale and QLS-31 scores of the both groups are demonstrated in table 7 and no significant difference between the two groups of patients' scores pre-therapy ($p>0.05$). Post-therapy, the qualities of life scores were significantly elevated in both groups and were above in the study group versus the control group ($p<0.05$).

***Functional area score***

The results of the functional area scores of the two groups of patients at different time points are demonstrated in table 8 and no significant difference between the two groups of patients' scores pre-therapy ($p>0.05$). Post-therapy, the functional area scores of patients in both groups were significantly higher and the study group was above to the control group ($p<0.05$).

***Clinical efficacy***

The results of the comparisons of the clinical efficacy of the both groups are demonstrated in table 9 and the overall effective rate of the study group was higher than that of the control group ($p<0.05$).

***Incidence of adverse reactions***

Patients in both groups experienced varying degrees of adverse reactions during treatment as demonstrated in table 10. No significant difference in the incidence of adverse reactions of diarrhoea and nausea and vomiting symptoms between the two groups ($p>0.05$). The incidence of adverse reactions with symptoms of gastrointestinal cramps and headache was significantly higher in the control group than the study group ($p<0.05$). The overall incidence of adverse reactions was significantly lower in the study group than the control group ($p<0.05$).

## DISCUSSION

The majority of patients with meningitis improve completely with active treatment and have a good clinical prognosis. However, if the disease is not treated appropriately or is more severe, the central nervous system is often involved and symptomatic epilepsy can occur (Dharmana *et al*., 2025; Taha, 2020). Its pathogenesis may be due to viral infections such as respiratory tract infections, skin and mucous membrane infections and intestinal infections, which enter the nerve tissue along the nerve endings through the blood circulation, invade the medial frontal lobe structures and affect the prefrontal cortex and temporal lobe, resulting in lesions of the centre nervous systems, or even necrosis of the brain parenchyma, affecting brain metabolism, which may in turn cause symptomatic epilepsy (Suryadevara, 2019). Patients suffer from sensory, motor, consciousness, mental and other disorders during seizures and seizures impair patients' physical, psychological and social functions, seriously reducing their quality of life. The cause of the disease is complex, in which the central nervous system damage caused by traumatic brain injury and cerebrovascular disease is the main cause. The involuntary convulsions, numbness of the limbs and pins and needles sensation that occur during the seizure may be accompanied by pallor, flushing of the whole body and blurring or loss of consciousness, which is extremely harmful (Yeager *et al*., 2020). Meningitis-associated epilepsy can further impair cognitive function and if the symptomatic epilepsy is persistent, it can lead to permanent brain damage, which can have a serious impact on the patient's long-term prognosis and qualities of life (Abdulaziz *et al*., 2020). Therefore, at the onset of this complication, systematic scientific treatment needs to be given in a timely manner in order to guarantee the therapeutic effect, prevent the emergence of sequelae and improvement of patients' qualities of life.

Traditional Chinese medicine classifies meningitis-associated epilepsy as a category of 'panic wind' and the cause of the disease is mainly due to insufficient qi and blood, siltation of the brain and marrow loss, etc., so the patient has symptoms such as loss of support for the tendons and veins, convulsions and spasms (Liang *et al*., 2024). The patient's condition is acute, mainly manifested as fever, irritability, coma and other symptoms, if not actively and effectively treated, it will lead to sequelae of the patient's neurological function and must be treated with drugs in a timely manner and the commonly used clinical treatment options are antibiotics, glucocorticosteroids and other drugs (Tian *et al*., 2022). With the in-depth research on the treatment of meningitis-associated epilepsy, many scholars consider the use of Chinese medicine drug treatment, such as Xiao Chai Hu Tang *et al* (W Liu *et al*., 2024; Su *et al*., 2024).

Sodium valproate is a broad-spectrum antiepileptic drug, the indications are primary generalised seizures, tonic-clonic seizures, apoplectic seizures, myoclonic tonus,

dystonic seizures, as well as partial seizures and other types of epilepsy. In addition, the drug also has an analgesic effect, for the nerve mechanism caused by migraine, can achieve certain results; can also play a role in emotional regulation and neurological stabilisation, to assist in the treatment of depression, anxiety also has good results (Z Ji *et al*., 2022). In this study, Xiao Chai Hu Tang plus minus Tang combined with sodium valproate was used to treat meningitis-associated epilepsy, which effectively prevented the transmission of the disease and achieved early treatment of the disease through the combined traditional Chinese medicines and western medicines.

The outcomes of this research revealed that all the indexes of patients in both groups were both superior to the pre-therapy in the treatment period. Post-therapy, the TCMS scores of the study group were substantially above the control group ($p<0.05$). Sodium valproate, as a commonly used antiepileptic drug, can play a role in inhibiting the excitability of neurons, promote γ-aminobutyric acid synthesis and contribute to the increase of inhibitory neurotransmitter concentration, effectively controlling and controlling epileptic seizures and improving the cerebral nerve function (Hakami, 2021). The cerebrospinal fluid has the function of cushioning, mitigating and eliminating damage to brain tissue from external forces and regulating intracranial pressure (Menéndez González, 2023), the comparison of the results of the proportion of returning to normal within 7d was above in study group to control group ($p<0.05$). Post-therapy, the levels of BDNF, NGF, IgM, IgG, IgA in study group patients were above to control group and the levels of TNF-α, IL-1β, IL-6 were below to control group. Seizures are related to the lowering of the body's immune ability and the patients' brain cells are hypoxic, which impairs the neural function and reduces the level of neurofactors, meanwhile, the patients' glial cells function abnormally, which induces the release of inflammatory factors, leading to the increase of inflammatory factor levels, such as TNF-α elevates the activity of glutamate, which induces epilepsy and IL strengthens the function of the glutamatergic neurons, which prolongs the duration of the seizure. Therefore neurofactors, inflammatory factors and immune function need to be monitored (Löscher and Howe, 2022; Soltani Khaboushan *et al*., 2022). The conclusion of this finding reveals that the Xiao Chai Hu Tang plus minus Tang combining valproate in treating meningitis-associated epilepsy could promote the improvement of neurological function, inhibit seizures and improve the levels of neurological and inflammatory factors in patients. This is because Chai Hu, Radix Rehmanniae Glutinosa, Radix Glycyrrhizae Praeparata, Ju Fang Zhi Bao San and Milkvetch Root in Xiao Chai Hu Tang Plus Minus Tang are able to reconcile the surface and the interior of the body, dispel cold and heat, relieve the liver, quench thirst, remove heat and toxins and effectively reduce inflammation and reduce convulsions (Huang *et al*., 2022; Ma *et al*., 2024). Lin and Hsieh (2021) reported in a review of Chinese herbal medicine for epilepsy that Chinese herbs such as Chai Hu have hepatoprotective, antitumour, antioxidant, antidepressant, anti-inflammatory and anticonvulsant effects, which can lessen the seriousness and durations of the seizure. This is consistent with the findings of this study.

Post-therapy, the recovery of epileptic symptoms was effectively assessed by the scale of activities of daily living (ADL) and the QLS-31 in epileptic patients (Gutiérrez-Viedma *et al*., 2021), which were above in study group to control group, while the functional area scores increased gradually in both groups and were above in study group to control group ($p<0.05$). Meanwhile, the functional area scores of two groups gradually elevated and the study group above the control group ($p<0.05$). It indicates that Xiao Chai Hu Tang plus minus Tang combined with sodium valproate treatment can contribute to the improvement of patients' cognitive function and enhance their ability to live and quality of life. This may be due to the fact that Acacia Sinensis and Zi Xue San in Xiao Chai Hu Tang Plus Minus Tang are capable of relieving depression and tranquillising the mind, regulating qi and opening up the stomach, stopping fright and calming the mind (Behera *et al*., 2024; Zhang *et al*., 2024). Codonopsis Pilosulae and Radix Glycyrrhizae Praeparata in the Tang belong to the tonic herbs, which can tonify the spleen and lung qi, nourish blood, produce fluids, increase immunity and benefit the intellect, which can improve the patient's ability to live and quality of life (L He *et al*., 2023; H Ji *et al*., 2022).

Furthermore, the overall clinical effectiveness rates of study group were above the control group post-therapy ($p<0.05$). No significant difference in the incidence of adverse reactions such as diarrhoea, nausea and vomiting between the two groups, the incidence of adverse reactions such as gastrointestinal cramps and headache in the study group was significantly lower than that in the control group and the overall incidence of adverse reactions in the study group was significantly lower than the control group ($p<0.05$), which may be caused by individual differences and other reasons. These results indicate that the short-term therapeutic effect of Xiao Chai Hu Tang Plus Minus Tang combined with sodium valproate in the treatment of meningitis-associated epilepsy is better than that of sodium valproate alone, which can effectively inhibit the release of patients' inflammatory factors and improve the patients' quality of life and provides a new therapeutic reference for the short-term clinical treatment of this disease. Some studies have shown that Xiao Chai Hu Tang can effectively reduce the inflammatory effect, enhance the immune function, improve the clinical efficacy and quality of life and reduce the adverse effects in patients with advanced lung cancer (Qingfeng *et al*., 2019). It has been shown that Xiao Chai Hu Tang improves the quality of life and reduces the incidence of adverse events in patients with cancer-

related fever (Bu *et al*., 2024). These findings are similar to those of the present study.

There are some limitations to this study. The sample size was relatively small, which may lead to biased results and affect the extrapolation and reliability of conclusions. Regarding the adverse effects in the adverse effects, the statistical comparison of the adverse effects may be somewhat biased due to individual differences and subjective factors. In addition, the observation period is short, whereas long-term treatment effects are crucial for a comprehensive understanding of treatment effects and the development of scientific treatment strategies.

## CONCLUSION

In this study, the treatment of meningitis-associated epilepsy by Xiao Chai Hu Tang Plus Minus Tang combined with sodium valproate, the results showed that this treatment method could effectively improve the TCMS scores, the proportion of cerebrospinal fluid restored to normal within 7d, neurological factors, immune function, functional area scores, quality of life and total clinical efficiency and reduce the levels of inflammatory factors and the total incidence of adverse reactions, which indicated that the efficacy of the combination of the two is accurate and provides a new reference method for relevant clinical treatment. However, this study has the shortcomings of small sample size and short treatment period; due to the condition limitation, it failed to include more specific inflammatory indexes such as others. Multi-centre, large-sample, high-quality clinical studies can be carried out in the future for validation.

***Conflicts of interest***

The authors declare that they have no financial conflicts of interest.

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