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# Efficacy and Safety Evaluation of Levetiracetam + Oxcarbazepine in the Treatment of Patients with Epilepsy Secondary to Stroke

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**Abstract:** *Objective*: To evaluate the therapeutic efficacy of levetiracetam (LEV) + oxcarbazepine (OXC) for post-stroke secondary epilepsy (PSE) in the elderly. *Methods*: 92 patients with PSE admitted to the hospital between July 2021 and July 2023 were selected. Random number table grouping was used, with 46 cases in the combination group, selecting LEV + OXC treatment; and 46 cases in the conventional group, selecting OXC treatment, comparing the treatment effect of the two groups. *Results*: The total effective rate of the combination group was higher than that of the conventional group, and the difference was statistically significant ($P < 0.05$). Before treatment, in the comparison of the epilepsy-related indexes and blood indexes between the groups, the difference was not statistically significant ($P > 0.05$). After treatment, the epilepsy-related indicators as well as blood indicators of the combination group were better than those of the conventional group, and the difference was statistically significant ($P < 0.05$). The adverse reaction rate of the combination group was lower than that of the conventional group, and the difference was statistically significant ($P < 0.05$). *Conclusion*: Implementing LEV + OXC therapy for PSE patients can enhance the effectiveness, improve the degree of epilepsy, regulate the blood indexes, and have high therapeutic safety.

**Keywords:** Levetiracetam; Oxcarbazepine; Post-stroke secondary epilepsy; Effectiveness; Safety

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## 1. Introduction

Post-stroke secondary epilepsy (PSE) is a highly prevalent disease in the elderly population, mostly secondary to stroke, and is characterized by sudden onset and recurrent seizures, which can severely damage the neuronal cells of patients, impacting the function of the nervous system. The common treatment for this disease is oral medication, with oxcarbazepine (OXC) being the most commonly used, which is capable of exerting antiepileptic efficacy and relieving the symptoms of the disease. However, the monotherapy effect of this drug is general, and the safety is not good [1]. Levetiracetam (LEV) belongs to the same antiepileptic drugs, and it has inhibitory properties for neurons in the hippocampal CA1 area, which can reduce the frequency of abnormal neuronal discharges, and then enhance the therapeutic efficacy. For this reason, 92 PSE patients were selected

in this study to evaluate the therapeutic efficacy of LEV + OXC.

## 2. Information and methods

### 2.1. General information

The study period was from July 2021 to July 2023, and 92 PSE patients were selected. Random number table grouping was used, with 46 cases in the combined group, consisting of 25 male patients and 21 female patients; with an age range from 62 to 89 years, mean 67.53 ± 2.18 years; disease duration range from 1 to 9 years, mean 5.19 ± 0.75 years. In the conventional group, there were 46 cases, with 26 male patients and 20 female patients; the age range was from 63 to 87 years old, mean 67.72 ± 2.35 years; the duration of the disease ranged from 1 to 8 years, mean 5.23 ± 0.64 years. A comparison of the basic data of the two groups showed no statistically significant difference ($P > 0.05$).

### 2.2. Methods

The conventional group chose OXC treatment with an initial dose of 4 to 5 mg/kg per dose, administered twice daily. The incremental dosage method was implemented, and the dosage was increased once every 1 week, each dose could not exceed 600 mg, and the dose was maintained at 600 to 2400 mg per day. The drug was used continuously for 6 months.

The combination group chose LEV + OXC treatment, and the therapy of OXC was the same as above. The initial dose of LEV was 500 mg per administration, twice daily. After 1 month of continuous use, the dose was 1000 mg per administration, twice daily, with 6 months of continuous use.

### 2.3. Observation indexes

Epilepsy-related indexes: record the number of seizures, electrocardiography conditions, duration of epilepsy, and epileptiform discharges.

Blood indexes: venous blood (fasting) was extracted and processed by centrifugation for 5 minutes at a rotational speed of 3,000 r/min. The supernatant was extracted, and the levels of S100 calcium-binding protein-β (S100-β), neuron-specific enolase (NES), interleukin-6 (IL-6), and IL-2 were measured by double-antibody sandwich enzyme-linked immunoassay.

Adverse reaction rate: observe the occurrence of rash, dizziness, vomiting, hair loss, drowsiness, and fatigue.

### 2.4. Efficacy evaluation criteria

Clinical cure: no seizures, able to participate in work or housework normally.

Significant effect: the daily seizure frequency is reduced by more than 80%.

Initial efficacy: daily seizure frequency reduction between 45% and 79%.

No efficacy: daily seizure frequency reduction did not reach 45%.

### 2.5. Statistical methods

The data were processed by SPSS 28.0 software, and the *t*-value was used to compare and test the measurement data, the $x^2$ value was used to compare and test the count data, and $P < 0.05$ was regarded as a statistically significant difference (**Table 1**).

**Table 1.** Comparison of the total effective rate of the two groups [n/%]

| Groups | Clinical cure | Significant effect | Initial efficacy | No efficacy | Total effectiveness |
|---|---|---|---|---|---|
| Combination group ($n$ = 46) | 21 (45.65) | 15 (32.61) | 8 (17.39) | 2 (4.35) | 95.65 (44/46) |
| Conventional group ($n$ = 46) | 16 (34.78) | 14 (30.43) | 7 (15.22) | 9 (19.57) | 80.43 (37/46) |
| $x^2$ | - | - | - | - | 5.060 |
| $P$ | - | - | - | - | 0.025 |

# 3. Results

## 3.1. Comparison of the total effective rate of the two groups

The total effective rate of the combined group is higher than that of the conventional group, and the difference is statistically significant ($P < 0.05$).

## 3.2. Comparison of epilepsy-related indicators between the two groups

Before treatment, the epilepsy-related indexes of the two groups were compared, and the difference was not statistically significant ($P > 0.05$). After treatment, the epilepsy-related indexes of the combined group were better than those of the conventional group, and the difference was statistically significant ($P < 0.05$). See **Table 2.**

**Table 2.** Comparison of epilepsy-related indexes in the two groups [mean ± SD]

| Groups | Number of seizures (times/year) | | Electrocardiography conditions (180/s) | | Seizure duration (min) | | Seizure-like discharges (180/s) | |
|---|---|---|---|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Combination group ($n$ = 46) | 2.59 ± 0.37 | 1.12 ± 0.25 | 6.98 ± 1.27 | 4.05 ± 0.37 | 4.39 ± 0.47 | 3.01 ± 0.25 | 15.79 ± 2.32 | 9.02 ± 1.25 |
| Conventional group ($n$ = 46) | 2.61 ± 0.41 | 1.53 ± 0.29 | 6.97 ± 1.25 | 4.88 ± 0.45 | 4.42 ± 0.49 | 3.59 ± 0.29 | 15.84 ± 2.36 | 10.89 ± 1.32 |
| $t$ | 0.246 | 7.263 | 0.038 | 9.663 | 0.300 | 10.274 | 0.102 | 6.977 |
| $P$ | 0.807 | 0.000 | 0.970 | 0.000 | 0.765 | 0.000 | 0.919 | 0.000 |

## 3.3. Comparison of blood indicators between the two groups

Before treatment, the blood indexes of the two groups are compared with each other, and the difference is not statistically significant ($P > 0.05$). After treatment, the blood indexes of the combined group are better than those of the conventional group, and the difference is statistically significant ($P < 0.05$), as shown in **Table 3**.

**Table 3.** Comparison of blood indexes between the two groups [mean ± SD]

| Groups | S100-β (μg/L) | | NES (IU/L) | | IL-6 (pg/ml) | | IL-2 (pg/ml) | |
|---|---|---|---|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Combination group ($n$ = 46) | 1.38 ± 0.53 | 0.42 ± 0.12 | 23.57 ± 3.24 | 11.45 ± 1.27 | 48.29 ± 4.19 | 16.35 ± 1.52 | 11.38 ± 2.16 | 3.84 ± 0.59 |
| Conventional group ($n$ = 46) | 1.39 ± 0.51 | 0.73 ± 0.18 | 23.48 ± 3.29 | 15.28 ± 1.34 | 48.24 ± 4.21 | 20.36 ± 1.58 | 11.39 ± 2.18 | 6.23 ± 1.27 |
| $t$ | 0.092 | 9.719 | 0.132 | 14.070 | 0.057 | 12.405 | 0.022 | 11.575 |
| $P$ | 0.927 | 0.000 | 0.895 | 0.000 | 0.955 | 0.000 | 0.982 | 0.000 |

### 3.4. Comparison of adverse reaction rates between the two groups

The adverse reaction rate of the combined group was lower than that of the conventional group, and the difference was statistically significant ($P < 0.05$), as shown in **Table 4**.

**Table 4.** Comparison of adverse reaction rates between the two groups [n/%]

| Groups | Rash | Dizziness | Vomiting | Hair loss | Drowsiness | Weakness | Incidence |
|---|---|---|---|---|---|---|---|
| Combination group ($n = 46$) | 0 | 1 (2.17) | 1 (2.17) | 0 | 0 | 0 | 4.35 (2/46) |
| Conventional group ($n = 46$) | 1 (2.17) | 2 (4.35) | 2 (4.35) | 1 (2.17) | 1 (2.17) | 1 (2.17) | 17.39 (8/46) |
| $x^2$ | - | - | - | - | - | - | 4.039 |
| $P$ | - | - | - | - | - | - | 0.045 |

## 4. Discussion

Epilepsy is a cerebral dysfunction caused by abnormal neuronal discharges in the brain, which is transient and sudden and affects the cognitive function of patients [2]. Stroke leads to abnormal sodium ion conductance in brain cells and cerebral ischemia, which in turn damages the depolarizing neurons and neighboring neurons, resulting in epileptic discharges. Antiepileptic drugs are commonly used for this condition and have therapeutic limitations as they reduce the frequency of epileptiform discharges and decrease the number of seizures, but they do not improve cognitive function in stroke patients.

OXC is a newer drug for PSE, which can block sodium channels, reduce their sensitivity to voltage, and then improve the cell membrane function of neurons, avoid repetitive neuronal discharges, inhibit the rapid propagation of synaptic impulses, and then play an antiepileptic role [3]. The drug has the activation of calcium ion channels, can enhance the conductivity of potassium ions, and then reduce the symptoms of the disease. However, the drug has more adverse reactions and the overall efficacy is average.

The target of LEV is synaptic vesicle protein 2A (SV2A), which is a glycoprotein covering 12 transmembrane domains and is widely distributed in the central nervous system and can regulate a variety of presynaptic neurotransmitters and synaptic vesicles, thereby reducing seizures [4]. The drug is highly selective, can play a dual mechanism, can be fast-acting, and the drug is better tolerated and can be combined with other antiepileptic drugs to enhance the efficacy of the treatment [5].

The results showed that the total effective rate of the combined group was higher than that of the conventional group. After treatment, the epilepsy-related indexes of the combined group were all better than those of the conventional group, the blood indexes were better than those of the conventional group, and the rate of adverse reactions of the combined group was lower than that of the conventional group, with a statistically significant difference ($P < 0.05$). The reason is that LEV can regulate a variety of receptors in the cerebral cortex so that they are widely distributed in the hippocampus, and have a protective effect on the central nervous system [6–7]. The drug has a long half-life of 6 to 8 hours. The half-life of the drug components in the cerebrospinal fluid can reach 12 to 16 hours. After acting on SV2A, it can effectively regulate the specific release of neural synaptic vesicles, thus inhibiting abnormal discharges. OXC, on the other hand, can act on electrically dependent ion channels and has regulatory properties for both calcium and sodium ion conduction processes, which can improve neurological function and synergistically exert antiepileptic effects [8–9]. The combination of the two drugs is highly selective and can regulate neuronal ion channels while maintaining the function of vesicle release, exerting the therapeutic effect in multi-targets and multi-channels, so the therapeutic effect is excellent [10–11]. The combination of drugs can reduce the dosage of OXC and reduce drug toxicity, so

there are fewer side effects.

In conclusion, LEV + OXC treatment for PSE patients can enhance the therapeutic efficacy, improve the epileptic performance of patients, regulate their physiological indexes, and is less likely to have adverse reactions.

## Disclosure statement

The authors declare no conflict of interest.

## References


[1] Zhang DL, Li AH, 2023, Effect Analysis of Levetiracetam Combined with Oxcarbazepine in the Treatment of Patients with Epilepsy Secondary to Stroke. Journal of Epilepsy and Neurophysiology, 32(5): 295–300.

[2] Wang SJ, Chen HR, Pan BY, 2023, Effectiveness of Butalbital Combined with Levetiracetam in the Treatment of Secondary Epilepsy after Stroke. Journal of Molecular Diagnosis and Therapy, 15(9): 1646–1649.

[3] Guo H, Qi SB, Zhou T, et al., 2020, Clinical and Literature Case Analysis of Levetiracetam-associated Thrombocytopenia. Journal of Adverse Drug Reactions, 22(12): 677–682.

[4] An TJ, 2021, Effectiveness and Safety Analysis of Oxcarbazepine Treatment for Secondary Epilepsy after Stroke. China Modern Drug Application, 15(5): 100–103.

[5] Bai YM, Du KX, Chen H, et al., 2023, Study on the Effects of Sodium Valproate, Oxcarbazepine, and Levetiracetam on the Development of Different Energy Zones in Children with Epilepsy as Assessed by the Chinese Version of the Griffiths Mental Developmental Assessment Scale. Chinese General Medicine, 26(23): 2918–2922.

[6] Xi GM, Chen ZD, 2023, Efficacy of Levetiracetam Tablets Combined with Oxcarbazepine Tablets in the Treatment of Epilepsy Patients and the Effects on Serum miR-222 and BAFF Levels. Hainan Medicine, 34(3): 318–321.

[7] Kang LL, Miao CY, Gao HF, 2023, Efficacy of Levetiracetam Tablets Combined with Oxcarbazepine Tablets in the Treatment of Epilepsy and the Effects on Serum miR-222 and BAFF Levels in Patients. Hainan Medicine, 34(5): 625–628.

[8] Guo LQ, Gui BS, 2022, Observation on the Effect of Different Drugs in the Combined Treatment of Post-stroke Seizures in the Elderly. Heilongjiang Medical Science, 45(1): 172–173.

[9] Qin Z, Ye F, Li YJ, et al., 2019, Analysis of the Effects of Antiepileptic Drug Monotherapy and Combination on the Efficacy, Prognosis, and Seizure Reoccurrence of Post-stroke Seizures in the Elderly. China Primary Medicine, 26(10): 1203–1207.

[10] Li CY, Xu LP, Wang SS, et al., 2023, Analysis of Retention and Effectiveness of Monotherapy with Different Antiepileptic Seizure Drugs in Post-stroke Epilepsy. Chinese Journal of Cerebrovascular Disease (Electronic Edition), 17(4): 325–330.

[11] Feng Q, Zhang B, Yi XY, et al., 2019, Study on the Retention Rate of Traditional and Novel Antiepileptic Drugs in Adult Patients with Epilepsy and the Interaction of Related Risk Factors. Chinese Journal of Modern Medicine, 21(1): 11–15.