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# Real-world Study of the Efficacy and Safety of Idebenone Tablets in the Treatment of Post-stroke Depression

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**Abstract:** *Objective:* This study aimed to systematically evaluate the effect of idebenone tablets in the treatment of post-stroke depression (Post-Stroke Depression, PSD). *Methods:* This study was a single-arm, prospective, observational study that recruited PSD patients who met the inclusion criteria after being assessed by the investigator between January 2022 and June 2023. The demographic characteristics, disease status, treatment status, and medication status of the patients were collected through questionnaires, and the Hamilton depression score of the patients was collected through the Case Report Form (CRF)to evaluate the effectiveness and safety of idebenone tablet treatment. *Results:* A total of 4902 PSD patients were included in this study, of which 2496 were males, accounting for 50.9%, and 2406 were females, accounting for 49.1%. According to the Hamilton Depression Rating Scale (HAMD), 13.9% were no depression at the first visit, 53.0% were mildly depressed, 24.3% were moderately depressed, and 8.8% were severely depressed. After treatment, the proportion of no depression was 26.1%, mild depression accounted for 53.3%, moderate depression accounted for 16.8%, and severe depression accounted for 3.8%, and the difference in the proportion of depression before and after treatment was statistically significant ($P$<0.05). *Conclusion:* Idebenone tablets can significantly reduce Hamilton's depression score, suggesting that it has a significant therapeutic effect in improving PSD symptoms.

**Keywords:** Post-stroke depression; Idebenone; Hamilton depression score; Real-world study

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## 1. Introduction

Post-stroke depression (PSD) is one of the common complications caused by stroke, with a high incidence of 30% to 50%, and a heavy burden of disease, affecting the long-term prognosis of patients. The pathological mechanism of PSD is complex, including inflammatory responses, neurochemical disorders after brain injury, and decreased

neuroplasticity. In view of the complex pathogenesis, the current treatment effect is very limited, and there is an urgent need to find new therapeutic agents to improve the long-term prognosis of patients. Previous studies have suggested that mitochondrial dysfunction affects the synthesis, release, and reuptake of neurotransmitters, which may lead to the development of depressive mood.

The CoQ10 antioxidant Idebenone has a unique anti-inflammatory, antioxidant, and improved mitochondrial function. Studies have shown that idebenone can protect nerve cells, reduce oxidative stress, and promote mitochondrial energy metabolism, thereby playing a therapeutic role in neurological diseases. In recent years, the application of idebenone in stroke rehabilitation has attracted much attention, especially in the treatment of PSD. However, research on the efficacy and safety of idebenone in PSD is still limited, especially with the insufficient real-world study.

Based on this, this study aims to systematically evaluate the efficacy and safety of idebenone tablets in the treatment of PSD through real-world studies. Through a larger sample size. This study hopes to provide strong evidence for the clinical application of idebenone in the treatment of PSD, and further explore its role in improving patients' psychological status and promoting neurorehabilitation. This not only helps to enrich the treatment strategy for PSD but also provides an important reference for clinicians to develop personalized treatment plans.

## 2. Data and methods

### 2.1. Study design

This study is a single-arm, prospective, observational study that aims to provide real-world data support for the rational use of idebenone tablets in clinical practice [1,2]. This study recruited patients with PSD who attended the clinic between January 2022 and June 2023 and met the inclusion and exclusion criteria after being assessed by the investigator. Idebenone tablets were administered orally, with a dose of 30 mg per time, three times daily after meals, for a continuous treatment period of 3 months. Follow-up assessments were conducted at baseline (before treatment) and after 3 months of treatment. The demographic characteristics, disease status, treatment, and medication of the patients were collected through questionnaires, and the Hamilton depression score of the patients was collected through the Case Report Form (CRF) to evaluate the effectiveness and safety of idebenone tablets [3].

### 2.2. Study population

The study intends to include PSD patients who have used idebenone tablets, and the specific screening criteria are as follows. Inclusion criteria: (1) Age ≥ 18 years old; (2) History of stroke confirmed as ischemic or hemorrhagic stroke within 6 months to 5 years of onset; (3) Depressive symptoms meet the diagnostic criteria for PSD in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or the International Classification of Diseases (ICD-10); (4) Patients or their family members voluntarily participate in this study and sign the informed consent form [4].

Exclusion criteria: (1) Presence of other serious neurological diseases, such as Alzheimer's disease, Parkinson's disease, epilepsy, etc.; (2) Patients with serious cardiovascular diseases, such as acute myocardial infarction, severe arrhythmia or heart failure, which may affect the safety evaluation of the study drug; (3) Patients with a history of schizophrenia, bipolar disorder or other serious mental illnesses; (4) Patients with severe abnormalities in liver or kidney function, which affect drug metabolism or may lead to aggravation of adverse reactions; (5) Patients who are participating in other interventional clinical trials or have received other

antidepressant treatments with uncertain efficacy within 3 months before treatment; (6) Patients with a history of allergy to idebenone or its components [5].

### 2.3 Evaluation index Hamilton depression score

(1) Hamilton Depression Score: The Hamilton Depression Rating Scale (HAMD) is a clinical scale compiled by Max Hamilton in 1960 to assess the severity of depression and is widely used in clinical diagnosis, efficacy evaluation and research. This scale is simple and reliable, and is a common tool in clinical research on depression. The scale consists of depressed mood, sensory loss, somatic symptoms, cognitive symptoms, anxiety symptoms, and suicidal ideation, with each item ranging from 0 to 4 points based on severity, with a total score ranging from 0 to 52 points. Typically, higher scores indicate more severe depressive symptoms. In this study, a score of 0–7 was no depression; 8–17 is mild depression; 18–24 indicates moderate depression; A score of 25 and above is severe depression.

(2) Evaluation of medication adherence: In this study, all patients were surveyed for their compliance with idebenone through a unified questionnaire, and whether the drug was discontinued and the reasons for discontinuation were recorded [6].

### 2.4. Statistical methods

Statistical analysis was performed using SAS 9.4 software. The mean and standard deviation of the quantitative data were described, and self-comparison was performed using the paired *t*-test/Wilcoxon signed-rank test or McNemar's test (for categorical variables). Analysis of variance (ANOVA) was used to compare the data among multiple groups. The frequency and rate were described by qualitative data, and the chi-square or McNemar's test was used for comparison between groups. The difference in hypothesis testing with a $P < 0.05$ was statistically significant [7,8].

## 3. Results

### 3.1. General demographic data of patients

A total of 4902 PSD patients were included in this study, including 2496 males (50.9%) and 2406 females (49.1%). More than 80% of the included PSD patients had bad lifestyle habits, as shown in **Table 1**.

### 3.2. The patient's stroke history and previous treatment methods

The duration of stroke varies, with only 0.1% of patients having been sick for less than 1 year, 49.5% having been sick for 1–2 years old, 24.4% having been sick for 2–3 years old, 18.6% having been sick for 3–5 years old, and 7.4% having been sick for more than 5 years old. More than 90% of the patients were treated with medication, 35.1% of the patients were treated with rehabilitation training, and 11.8% of the patients were treated with surgery, as shown in **Table 2**.

**Table 1.** General demographic data of patients [n,(%)]

| Variable | Patients with PSD (*n* = 4902) |
|---|---|
| Gender | |
| Male | 2496 (50.9) |
| Female | 2406 (49.1) |
| Age | |
| < 18 years old | 24 (0.5) |
| 18–30 years old | 110 (2.2) |
| 31–40 years old | 257 (5.2) |
| 41–50 years old | 469 (9.6) |
| 51–60 years old | 1145 (23.4) |
| 61–70 years old | 1371 (28.0) |
| 71–80 years old | 1014 (20.7) |
| > 80 years old | 512 (10.4) |
| Family history | |
| Yes | 681 (16.8) |
| No | 3385 (83.2) |
| Hypertension | |
| Yes | 2901 (59.2) |
| No | 2001 (40.8) |
| Diabetes | |
| Yes | 1076 (22.0) |
| No | 3826 (78.0) |
| Dyslipidemia | |
| Yes | 1353 (27.6) |
| No | 3549 (72.4) |
| Heart disease | |
| Yes | 588 (12.0) |
| No | 4314 (88.0) |
| Vasculitis | |
| Yes | 160 (3.3) |
| No | 4742 (96.7) |
| Bad living habits | |
| Yes | 3995 (81.5) |
| No | 907 (18.5) |

**Table 2.** Stroke history and previous treatment methods [n,(%)]

| Variable | Statistics |
|---|---|
| Duration of stroke | |
| < 1 year | 7 (0.1) |
| 1–2 years | 2423 (49.5) |
| 2–3 years | 1193 (24.4) |
| 3–5 years | 912 (18.6) |
| > 5 years | 365 (7.4) |
| Prior medication | |
| Yes | 4617 (94.2) |
| No | 285 (5.8) |
| Rehabilitation training treatment | |
| Yes | 1719 (35.1) |
| No | 3183 (64.9) |
| Surgical treatment | |
| Yes | 576 (11.8) |
| No | 4326 (88.2) |

### 3.3. Changes in the distribution of depression before and after treatment

According to the Hamilton Depression Scale, 13.9% had no depression at the first visit, 53.0% were mildly depressed, 24.3% were moderately depressed, and 8.8% were severely depressed. After treatment, the proportion without depression was 26.1%, mild depression accounted for 53.3%, moderate depression accounted for 16.8%, and severe depression accounted for 3.8% and the difference in the proportion of depression before and after treatment was statistically significant ($P < 0.05$) (**Table 3**).

**Table 3.** Changes in the distribution of depression before and after treatment [n,(%)]

| | No depression | Mild depression | Moderate depression | Severe depression |
|---|---|---|---|---|
| First diagnosis | 682(13.9) | 2596(53.0) | 1192(24.3) | 432(8.8) |
| After treatment | 1279(26.1) | 2613(53.3) | 824(16.8) | 186(3.8) |
| $\chi^2$ | | 345.462 | | |
| $P$ | | <0.05 | | |

### 3.4. Drug adherence analysis

During the treatment, 3.1% of the patients had self-discontinuation, and the reasons for self-discontinuation were: inconvenient follow-up (67 people, accounting for 43.5%), and poor self-perception (55 people, accounting for 35. 7%), adverse reactions (17 people, accounting for 11.0%) and others (15 people, accounting for 9.8%) (**Table 4**).

**Table 4.** Analysis of drug adherence [n,(%)]

| Variable | Statistics |
|---|---|
| Whether to stop taking the drug | |
| Yes | 154 (3.1) |
| No | 4748 (96.9) |
| Reasons for drug discontinuation (154 people stopped taking the drug) | |
| Inconvenient follow-up examination | 67 (43.5) |
| Feeling ineffective | 55 (35.7) |
| Adverse reactions were severe | 17 (11.0) |
| Other | 15 (9.8) |

## 4. Discussion

In this study, we evaluated the efficacy of idebenone tablets in patients with PSD, and the results showed that idebenone tablets significantly reduced Hamilton's depression score, suggesting that it had a significant therapeutic effect in improving PSD symptoms. The results of the study further support the use of idebenone as an effective intervention for PSD patients, which not only provides a new option for clinical treatment but also provides a basis for the development of subsequent large-scale and multi-center clinical trials.

In this study, although idebenone tablets had a significant improvement in the Hamilton depression score of post-stroke depressed patients, 3.1% of patients still self-stopped the drug, and the inconvenience of follow-up visits was the largest among patients who stopped taking the drug. This discontinuation rate is relatively low compared to previous studies. In a previous study [9], the discontinuation rate of antidepressants for PSD was

between 7% and 30%, mainly due to drug infeasibility or more drug side effects. The discontinuation rate in this study was relatively low, which suggests that idebenone is tolerable and safe, indicating that it has better patient compliance and acceptance in practical clinical applications. This result further supports the potential advantages of idebenone in the treatment of PSD.

PSD is a common serious complication that not only increases the mental burden of patients and reduces their quality of life, but also increases the risk of recurrence and death after stroke. Although several drugs are currently used to treat PSD, their efficacy and safety still have certain limitations [10]. As a drug with strong antioxidant and mitochondrial protective effects, idebenone can promote the recovery of brain tissue by scavenging free radicals, reducing apoptosis, and improving neuronal function, thereby relieving depressive symptoms. In addition, idebenone may further exert its antidepressant effects by regulating the metabolic balance of neurotransmitters, improving cerebral blood flow, and energy metabolism. These mechanisms suggest that idebenone has unique advantages in the treatment of PSD [11].

Some limitations are inevitable in this study. First, the observation time of this study is short, and the effect of idebenone tablets on the long-term efficacy and safety of post-stroke depressed patients cannot be fully evaluated. In addition, this study did not conduct an in-depth analysis of the reasons for patient self-discontinuation, and future studies should more comprehensively explore patient compliance, especially factors related to drug side effects or individual differences. These limitations suggest that larger, multicenter, long-term follow-up studies are needed before more definitive conclusions can be drawn [12].

## 5. Conclusion

In summary, the results of this study verify the effectiveness of idebenone tablets in improving PSD symptoms, especially in reducing Hamilton's depression score. Although this study has some limitations, such as the lack of a control group and short observation time, the results provide a strong basis for further exploring the application value of idebenone in PSD. Future studies should consider expanding the sample size, extending the follow-up time, and exploring the combination of idebenone with other treatments to further optimize the treatment strategy for PSD.

## Disclosure statement

The authors declare no conflict of interest.

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