

Effect of a combination of *Ginkgo biloba* leaf extract and triangle health management in patients with ischemic vertigo- An exploratory investigation

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Abstract: Background: Ischemic vertigo (IV) is the main clinical manifestation of posterior circulation ischemia. Extract of *Ginkgo biloba* leaves injection (EGBLI) is rich in flavonoids and terpene lactones, which have antioxidant, vasodilator and neuroprotective effects. Triangle Health Management optimizes resource allocation through hierarchical intervention. **Objectives:** This prospective study analyzed the effect of EGBLI combined with triangle health management on IV. **Methods:** First, n=177 patients with IV were included who received conventional treatment as a control group and another n=144 patients who received EGBLI as an observation group. The clinical efficacy of the two groups was compared and hemodynamics before and after treatment were examined. In addition, nutritional proteins and symptom improvement were compared between the two groups. **Results:** Comparison showed that the clinical efficacy of the observation group was better ($p<0.05$). Meanwhile, hemodynamics and symptom improvement after treatment in the observation group were better than those in the control group ($p<0.05$). **Conclusion:** EGBLI combined with triangle health management is an excellent therapeutic regimen for IV.

Keywords: Extract of *Ginkgo biloba* leaves injection; Hemodynamics; Ischemic vertigo; Nutritional status; Vascular endothelial function

Submitted on 23-08-2024 – Revised on 20-11-2025 – Accepted on 11-12-2025

INTRODUCTION

Vertigo, a main clinical symptom of posterior circulation ischemia (Shah *et al.*, 2023). According to the World Health Organization, ischemic vertigo (IV) affects up to 50-60% of people over 65 years of age, with an average incidence of 5-8% across all age groups (Beretti and Desnous, 2023). IV is characterized by disorders of orientation and spatial balance, often accompanied by tinnitus and slow movement, which may resolve after rest but can lead to delayed diagnosis (Yao and Zu, 2023). In severe cases, IV progresses to brain infarction, causing disability or death (Eggers, 2021). Clinically, IV is linked to malnutrition, with obesity and poor diet identified as key risk factors (Bronstein and Kattah, 2024). Thus, IV treatment should address both cerebrovascular hemodynamics and nutritional status to achieve optimal outcomes.

Traditional IV therapies commonly use calcium ion antagonists and vasodilators. Their mechanism involves improving cerebral blood circulation while protecting cerebral nerves; however, this approach is often suboptimal due to significant adverse effects and high recurrence rates (Deng *et al.*, 2022). In contrast, *Ginkgo biloba* leaf extract (EGBLI) represents a natural alternative rich in bioactive compounds, including ginkgo flavonol glycosides (e.g., quercetin-3-O-rutinoside) and terpene lactones (e.g., ginkgolides). These components exhibit free radical scavenging activity, vasodilation via prostaglandin

modulation and neuroprotection through Sirtuin 1 (SIRT1) pathway activation (Liu *et al.*, 2022). Chemically, the sulfonation of flavonoid glycosides in EGBLI enhances its water solubility and bioavailability, facilitating synergistic effects with management strategies like triangle health management (Yu *et al.*, 2024). This study hypothesized that EGBLI's multimodal bioactive profile (flavonoids-mediated antioxidation, terpenoids-induced vasodilation) could synergize with Triangle Health Management's precision interventions. Flavonoids like quercetin-3-O-rutinoside have been shown to cross the blood-brain barrier (Hasan *et al.*, 2023), potentially enhancing the cognitive benefits of balance training. Terpene lactones may amplify the neuroplasticity effects of environmental modifications (Kitajima *et al.*, 2025). This dual-action mechanism addresses both hemodynamic dysfunction (targeted by EGBLI) and sensorimotor adaptation (addressed by triangle management).

Therefore, this exploratory study aims to investigate the synergistic mechanism of EGBLI and triangle health management in IV treatment, focusing on hemodynamic, nutritional and functional outcomes. This study hypothesizes that EGBLI's chemical properties potentiate the management model's efficacy, offering a novel integrated approach for IV.

MATERIALS AND METHODS

Subjects

This study was conducted at The First Affiliated Hospital

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of Soochow University, Suzhou, Jiangsu, China. This prospective study analyzed patients with IV admitted to The First Affiliated Hospital of Soochow University from January 2024 to June 2024.

The sample size was calculated a priori using G*Power software (version 3.1). With an effect size of 0.5, alpha of 0.05 and power of 0.8, the minimum required sample size was n=114 per group. This study enrolled n=177 controls and n=144 observations to account for potential dropouts and ensure robust analysis.

After screening based on inclusion/exclusion criteria, n=321 patients were enrolled. To minimize bias, patients were allocated using computer-generated random numbers and outcome assessors were blinded to group assignments. However, due to the retrospective nature, full blinding of participants was not feasible. The control group (n=177) received conventional treatment (betahistine mesylate + basic health education), while the observation group (n=144) received additional EGBLI. The study was approved by the Ethics Committee of The First Affiliated Hospital of Soochow University (KL20240114) and conducted in accordance with the Declaration of Helsinki. Baseline data showed no significant differences (Table 1, $p>0.05$).

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients whose IV was in line with the diagnostic guidelines (Edlow *et al.*, 2023) and confirmed by imaging examination. (2) Patients who developed IV for the first time and received treatment at The First Affiliated Hospital of Soochow University. (3) Patients with complete medical records. (4) Patients > 18 years old.

Exclusion criteria: (1) Patients whose IV was caused by other reasons. (2) Patients who were unconscious. (3) Patients complicated with severe organ function damage. (4) Patients complicated with malignant tumors. (5) Patients complicated with stroke, traumatic brain injury, or hematological disorders.

Methods

Control group: Betahistine Mesilate (Eisai China Inc., H20040130, purity >99%), 6 mg orally three times daily for 4 weeks, plus basic health education (dietary advice and activity guidance).

Observation group: Conventional treatment + EGBLI (Youcare Pharmaceutical Group Co., Ltd., H20070226; composed of 24% flavonol glycosides and 6% terpene lactones, HPLC-grade). EGBLI (35 mg) was dissolved in 250 mL of 0.9% sodium chloride injection (Baxter Healthcare) and administered via intravenous infusion once daily for 4 weeks.

Triangle health management

Triangle health management: This is a stratified care model

adapted from Zeng *et al* (2022). that categorizes patients based on Dizziness Handicap Inventory (DHI) scores into three tiers

- Mild (DHI 0-29): Interventions included balance rehabilitation training (e.g., head movement, standing and visual balance exercises), psychological counseling (e.g., music therapy, attention diversion) and family support to alleviate emotional fluctuations.

- Moderate (DHI 30-59): Interventions included fall risk assessments, environmental hazard elimination, installation of protective barriers, health education for patients and families and self-protection training during vertigo episodes.

- Severe (DHI 60-100): Interventions recommended hospitalization, video-nystagmography-guided restoration maneuvers, bedside fall prevention signs, bedrails and assisted mobility with non-slip shoes and family accompaniment.

This protocol ensures tailored care based on severity, optimizing resource use and patient outcomes.

Clinical efficacy assessment

Clinical efficacy was evaluated concerning the treatment guideline for IV (Sanalp Menekse *et al.*, 2025). Cured: symptoms completely disappeared after treatment. Significantly effective: Symptoms significantly improved after treatment. Effective: Symptoms relieved after treatment. Ineffective: No changes in symptoms after treatment.

Outcome measures

(1) Clinical efficacy (2) Cerebral blood flow in patients measured by the color Doppler ultrasound before and after treatment, including the left and right vertebral artery and basilar artery. (3) Fasting venous blood was drawn from patients in both groups before and after treatment. Von Willebrand Factor (vWF), Thrombomodulin (TM) and Endothelin 1 (ET-1) were measured by ELISA and Albumin (ALB), Transferrin (TRF), Prealbumin (PAB) and Total protein (TP) by automatic biochemical analyzer. (4) Before and after the treatment, the Wolf Motor Function Test (WMFT) (Zhang *et al.*, 2021), Berg Balance Scale (BBS) (Joa, 2024) and Functional Independence Assessment (FIM) (Almeida Matos *et al.*, 2020) were performed. A higher score in WMFT, BBS and FIM indicated better motor ability, balance and independent living ability, respectively. (5) After the end of treatment, patient satisfaction was evaluated. A scale of 1-10 was used, with 10 being "very satisfied", 7-9 being "satisfied" and 1-6 being "unsatisfied" (Muhlbacher and Stolk, 2023).

Statistical analysis

SPSS 24.0 software was used for statistical analysis. Enumeration data were presented as (%) and were compared between groups using the chi-square test. Measurement data were expressed as ($\bar{\chi} \pm SD$), with an

independent sample t-test for comparison between groups and a paired t-test for intra-group comparison. Statistical significance was defined as $p < 0.05$

RESULTS

Comparison of clinical efficacy

None of the patients experienced any significant side effects (e.g., respiratory depression, coma, nausea and vomiting, allergy, etc.) during or after injection therapy. After statistical analysis, the total effective rate was 92.36% in the observation group and 84.18% in the control group ($p < 0.05$), table 2.

Comparison of hemodynamics

Compared to the conditions before treatment, the blood flow velocities in the left and right vertebral artery and basilar artery increased in both treatment groups ($p < 0.05$). However, intergroup comparison showed that the blood flow velocity in the observation group was higher than that in the control group ($p < 0.05$), (Table 3).

Comparison of vascular endothelial function

The vascular endothelial function indicators were significantly lower in both groups after treatment compared to those before treatment ($p < 0.05$), in which the vWF, TM and ET-1 in the observation group lower than those in the control group ($p < 0.05$), (Table 4).

Comparison of nutritional status

ALB, PAB, TRF and TP in the observation group after treatment were elevated and were higher than those in the control group ($p < 0.05$), (Table 5).

Comparison of the improvement in symptoms

The observation group, the WMFT, BBS and FIM scores were (65.03 ± 8.80), (54.19 ± 1.75) and (69.85 ± 9.83), respectively, showing more pronounced elevation compared to the control group ($p < 0.05$), (Table 6).

Comparison of treatment satisfaction

The satisfaction rate was 93.06% in the observation group and 89.27% in the control group ($p > 0.05$, Table 7).

DISCUSSION

This study demonstrates that EGBLI combined with Triangle health management significantly improves hemodynamics, nutritional status and functional scores in IV patients compared to conventional treatment alone. The total efficacy rate of 92.36% in the observation group (vs. 84.18% in controls) (Table 2-7) underscores the potential synergy between EGBLI's chemical actions and graded management.

In clinical practice, vertebral-basilar insufficiency is considered the main cause of IV; therefore, improving cardiovascular and peripheral circulatory conditions, dilating vertebral artery pressure and reducing its pressure

form the basis for IV treatment (Parfenov *et al.*, 2021). Traditional medicines (e.g., betahistine) have a pharmacological mechanism that includes strong thrombolytic effects, significant inhibition of platelet aggregation, reduction of blood lipid and viscosity within a short period, suppression of norepinephrine release and improvement of microcirculation (Choi *et al.*, 2023), which lays the foundation for IV treatment. This study showed that the hemodynamics of the observation group after treatment were better, and vWF, TM, and ET-1 were lower than those of the control group (Tables 3 and 4). EGBLI, as an extract of dried *Ginkgo biloba* leaves, exhibits biological activities in various domains; the active components contained, such as ginkgolides and flavonoid glycosides, can effectively promote prostaglandin synthesis, stimulate catecholamine secretion and scavenge oxygen free radicals, thereby improving microcirculation, reducing blood viscosity and promoting blood circulation (Q. Liu *et al.*, 2024). Similarly, it is also found that EGBLI protects osteoarticular cells by improving cellular energy metabolism (Liu *et al.*, 2023), which aligns with the view of this study. Furthermore, in a rat experiment, researchers found that EGBLI exhibits excellent antiplatelet aggregation and antithrombotic effects (Neri *et al.*, 2021), which are of significant importance in improving the pathological progression of IV.

The results of the nutritional status comparison showed that EGBLI had a positive effect on improving the nutritional status of the patients (Table 5). As mentioned above, the occurrence of IV is directly related to hemodynamics and dysregulation of blood lipids, blood glucose and endothelial function are major factors contributing to abnormal hemodynamic changes (Gunes-Bayir *et al.*, 2023). Therefore, the nutritional status of patients largely determines their recovery status. A previous study indicated that malnourished individuals are prone to recurrence with regard to the prognosis of IV (Cheng *et al.*, 2021). Consequently, clinical emphasis is placed on dietary guidance to patients during IV treatment to improve their nutritional status and ensure treatment efficacy (Wischmeyer *et al.*, 2024). Although drugs like betahistine are effective in improving the symptoms of IV, they do not affect the nutritional status of patients. On the contrary, although the primary effects of EGBLI rely on flavonoids and terpenoids contained, the impacts of its abundant polysaccharides, phenolic compounds, organic acids, alkaloids, amino acids, steroidal compounds, trace elements and other nutrients on the body's nutritional status should not be ignored (Zhao *et al.*, 2024). For instance, ester compounds improve cerebral blood flow and enhance the absorption of oxygen and nutrients by brain cells (Razna *et al.*, 2020). Essential micronutrients such as vitamins C and E and calcium also contribute to maintaining nutritional balance in the body, thereby further improving the efficacy of treatment and providing reliable support for long-term health outcomes.

Table 1: Comparison of clinical data.

	Control group (n=177)	Observation group (n=144)	t (or χ^2)	p
Age (years)	52.70±5.77	53.11±4.41	0.653	0.515
Sex			0.259	0.611
<i>male</i>	80 (45.20)	61 (42.36)		
<i>female</i>	97 (54.80)	83 (57.64)		
Duration of disease (months)	4.29±1.31	4.27±1.34	0.147	0.883
BMI (kg/m ²)	24.13±2.45	24.48±1.69	1.443	0.150
Combined hypertension			0.126	0.723
<i>yes</i>	76 (42.94)	59 (40.97)		
<i>no</i>	101 (57.06)	85 (59.03)		
Combined diabetes mellitus			0.141	0.707
<i>yes</i>	64 (36.16)	55 (38.19)		
<i>no</i>	113 (63.84)	89 (61.81)		
DHI	47.82±22.03	50.70±21.32	1.189	0.235

Note: Dizziness Handicap Inventory (DHI), Body Mass Index (BMI).

Table 2: Comparison of clinical efficacy.

Healing	Control group (n=177)	Observation group (n=144)	χ^2	p
Cured	14 (7.91)	24 (16.67)		
Significantly effective	65 (36.72)	56 (38.89)		
Effective	70 (39.55)	56 (38.89)		
Ineffective	28 (15.82)	11 (7.64)		
Total effective rate (Cured+Significantly effective +Effective)	84.18%	92.36%	4.978	0.026

Table 3: Comparison of hemodynamics.

Artery	Timing	Control group (n=177)	Observation group (n=144)	t	p
Left vertebral artery (cm/s)	Before-treatment	34.74±6.13	34.94±5.63	0.301	0.763
	After-treatment	39.35±5.44*	45.20±5.80*	9.357	<0.001
Right vertebral artery (cm/s)	Before-treatment	34.15±5.93	35.06±6.24	1.342	0.181
	After-treatment	37.18±5.11*	42.48±5.48*	8.997	<0.001
Basilar artery (cm/s)	Before-treatment	33.34±3.96	33.89±4.70	1.147	0.252
	After-treatment	35.62±5.50*	43.71±5.60*	13.080	<0.001

Note: * indicates $p < 0.05$ compared to before treatment.

Table 4: Comparison of vascular endothelial function.

Vascular endothelial function	Timing	Control group (n=177)	Observation group (n=144)	t	p
vWF (U/mL)	Before-treatment	1.66±0.48	1.58±0.40	1.602	0.110
	After-treatment	1.40±0.35*	1.29±0.25*	3.107	0.002
TM (ng/mL)	Before-treatment	1.87±0.33	1.83±0.23	1.142	0.254
	After-treatment	1.64±0.32*	1.42±0.23*	7.093	<0.001
ET-1 (ng/L)	Before-treatment	108.32±28.71	110.91±30.45	0.788	0.431
	After-treatment	99.77±24.57*	85.83±21.20*	5.409	<0.001

Note: * indicates $p < 0.05$ compared to before treatment. Von Willebrand Factor (vWF), Thrombomodulin (TM), Endothelin 1 (ET-1)

This is also the reason why WMFT, BBS and FIM were higher in the observation group than in the control group (Table 6). However, while nutritional biomarkers improved, direct causality to functional outcomes remains uncertain. Future studies should incorporate serum albumin kinetics and inflammatory cytokines (e.g., CRP) to elucidate metabolic pathways. The observed correlations

might reflect reverse causality, as improved mobility (measured by BBS) could independently enhance nutritional intake. Safety-wise, no significant adverse effects were reported, consistent with EGBLI's established profile (Yue *et al.*, 2024), but larger trials should monitor rare events.

Table 5: Comparison of nutritional status.

Nutritional proteins	Timing	Control group (n=177)	Observation group (n=144)	t	p
ALB (g/L)	Before-treatment	42.56±6.28	42.55±5.09	0.022	0.983
	After-treatment	42.83±5.95	45.21±5.84*	3.715	<0.001
PAB (mg/L)	Before-treatment	336.41±44.26	329.84±34.90	1.462	0.145
	After-treatment	333.81±41.33	345.63±31.19*	2.855	0.005
TRF (g/L)	Before-treatment	2.84±0.42	2.78±0.39	1.340	0.181
	After-treatment	2.84±0.43	3.20±0.46*	7.123	<0.001
TP (g/L)	Before-treatment	68.83±6.01	69.09±6.90	0.367	0.714
	After-treatment	69.09±6.62	73.52±6.12*	6.205	<0.001

Note: * indicates $p < 0.05$ compared to before treatment. Albumin (ALB), Transferrin (TRF), Prealbumin (PAB), Total protein (TP).

Table 6: Comparison of the improvement in symptoms.

Symptom score	Timing	Control group (n=177)	Observation group (n=144)	t	p
WMFT	Before-treatment	34.97±7.64	33.71±5.88	1.633	0.103
	After-treatment	47.65±9.31*	65.03±8.80*	17.160	<0.001
BBS	Before-treatment	44.98±3.57	44.52±2.63	1.296	0.196
	After-treatment	50.77±1.31*	54.19±1.75*	20.070	<0.001
FIM	Before-treatment	37.16±2.25	36.63±3.60	1.639	0.102
	After-treatment	53.99±7.55*	69.85±9.83*	16.410	<0.001

Note: * indicates $p < 0.05$ compared to before treatment. Wolf Motor Function Test (WMFT), Berg Balance Scale (BBS), Functional independence assessment (FIM).

Table 7: Comparison of treatment satisfaction.

Satisfaction	Control group (n=177)	Observation group (n=144)	χ^2	p
Very satisfied	79 (44.63)	69 (47.92)		
Satisfied	79 (44.63)	65 (45.14)		
Unsatisfied	19 (10.73)	10 (6.94)		
Satisfaction rate (Very Satisfied+Satisfied)	89.27%	93.06%	1.388	0.239

On the other hand, the triangle health management implemented in this study also has a certain impact on improving the recovery of patients. The role of triangle health management can be analyzed from the following three perspectives: (1) Nutritional intervention can reduce the nerve oxidative stress injury of patients. For example, previous studies have shown that low-fat diet reduces lipid peroxidation damage in the microcirculation of the inner ear labyrinth by reducing triglyceride levels (C. Y. Liu *et al.*, 2024). It is well known that IV is accompanied by significant endothelial dysfunction (increased vWF/ET-1 in the control group) and a high risk of thrombosis (Tong *et al.*, 2024). These help to maintain the stability of vascular endothelial function and ensure blood flow circulation in patients with IV. (2) Exercise intervention can improve the plasticity of neural function. According to the analysis of proprioceptive training reduces the vestibulospinal tract threshold by enhancing the sensitivity of plantar pressure receptors (Nakamura *et al.*, 2024). This ameliorating effect accelerated central adaptation to asymmetric vestibular input, which explained the improved dynamic balance (WMFT) and reduced fall risk in the observation group. (3) Environmental modifications (e.g., fall prevention signs) mitigated external stressors that exacerbated hemodynamic dysfunction. IV exacerbations

are often triggered by postural changes or visual-vestibular mismatches. Interventions can reduce vestibulo-ocular reflex overload through the installation of fall-prevention signs and mobility aids (e.g., non-slip shoes). These interventions with EGBLI will produce a series of synergies, such as EGBLI's antioxidant-rich flavonoids (e.g., quercetin-3-O-rutinoside) and terpene lactones, which synergize with nutritional interventions targeting endothelial function. Specifically, Triangle Health Management's emphasis on antioxidant-rich diets (e.g., polyphenol-rich fruits/vegetables) potentiates EGBLI's ability to reduce oxidative stress markers like vWF and ET-1. This aligns with evidence showing dietary flavonoids enhance eNOS activity and NO bioavailability in endothelial cells (Reis *et al.*, 2024). Secondly, balance rehabilitation training directly engages neuroplasticity pathways activated by EGBLI's terpenoids. Animal studies demonstrate that ginkgolides promote synaptic remodeling via CREB phosphorylation (Huang *et al.*, 2021), which is augmented by sensorimotor training-induced BDNF upregulation (Beier *et al.*, 2021). As a result, the satisfaction survey results from both groups of patients in this study were above 95% (Table 7), indicating the high clinical value of this approach.

However, several limitations warrant caution. First, the retrospective design and lack of full blinding may introduce selection bias. Second, the 4-week duration is insufficient to assess long-term outcomes such as recurrence rates or sustainability. Third, the sample size (n=321) may lack power for subgroup analyzes. Additionally, while nutritional biomarkers improved, direct causal links to functional scores (e.g., WMFT) remain speculative without controlling for confounding factors like diet. Future prospective studies with longer follow-up and biochemical validation (e.g., oxidative stress markers) are needed.

CONCLUSION

EGBLI combined with triangle health management improved hemodynamics, vascular function and nutritional status in IV patients over a 4-week period. The chemical properties of EGBLI, particularly its flavonoid and terpene components, likely contributed to these effects through mechanisms involving blood flow enhancement and oxidative stress reduction. However, the exploratory design and short duration limit generalizability. These findings support further investigation via randomized controlled trials to validate long-term efficacy and synergy mechanisms.

Acknowledgments

Not applicable.

Authors' contributions

Xiuqin Shen: Conceived and designed the project and wrote the paper; Ying Zhang: Generated the data; Jiao Wei: Analyzed the data; Xiuqin Shen: Modified the manuscript. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Funding

There was no funding

Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

The study was approved by the Ethics Committee of The First Affiliated Hospital of Soochow University (KL20240114) and conducted in accordance with the Declaration of Helsinki. This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflict of interest

The authors have no conflict of interest to declare.

Supplementary data

<https://www.pjps.pk/uploads/2026/04/SUP1776326429.pdf>

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