



The Role of Cytoflavin as Adjuvant Therapy in Acute Stroke in Evolution: A Case Report at Dr. Chasbullah Abdul Majid Regional Hospital, Bekasi City

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Track Record Article	Abstract
Revised: 20 June 2026 Accepted: 29 September 2026 Published: 30 September 2026 How to cite : Utomo, T. Y., Samosir, D. J., & Yudawijaya, A. (2026). The Role of Cytoflavin as Adjuvant Therapy in Acute Stroke in Evolution: A Case Report at Dr. Chasbullah Abdul Majid Regional Hospital, Bekasi City. <i>Contagion : Scientific Periodical of Public Health and Coastal Health</i>, 8(3), 632–643.	<i>Ischemic stroke results from reduced cerebral blood flow due to vascular occlusion, while Acute Stroke in Evolution (ASE) is characterized by progressive neurological deterioration during the acute phase. Cytoflavin has been proposed as an adjuvant neuroprotective therapy because of its potential to support cellular metabolism and tolerance to hypoxia; however, clinical evidence regarding its role in ASE remains limited, particularly in patients with multiple vascular risk factors. To document serial changes in neurological deficit, assessed using the National Institutes of Health Stroke Scale (NIHSS), and the safety of Cytoflavin as an adjuvant therapy in a single case of ASE with multiple risk factors. This was a prospective single-case report of a 38-year-old man with lacunar ischemic stroke managed at Dr. Chasbullah Abdul Majid Regional Hospital, Bekasi City. Clinical progression was evaluated through serial neurological examinations, NIHSS assessments, and head computed tomography (CT). The patient presented with sudden right-sided weakness, dysarthria, and facial deviation. His vascular risk factors included uncontrolled diabetes mellitus, hypertension, obesity, dyslipidemia, and smoking. The initial NIHSS score was 5, and head CT demonstrated a left basal ganglia lacunar infarction. On day four, neurological deficits worsened, with right-sided motor strength decreasing to 2/5 and the NIHSS score increasing to 12, consistent with ASE. Intravenous Cytoflavin 500 mg in 100 mL 0.9% NaCl three times daily was administered for 10 days. Neurological improvement began on day six. By day ten, motor strength improved to 5–, the patient was able to ambulate with mild hemiparesis, and the NIHSS score decreased to 4. The neurological improvement was temporally associated with the administration of Cytoflavin and comprehensive supportive management. No significant safety concerns were observed during treatment. In this single uncontrolled case of ASE, administration of Cytoflavin as an adjuvant therapy was temporally associated with improvement in neurological deficits, reflected by a reduction in NIHSS from 12 to 4 over 10 days. However, no causal inference can be drawn from a single uncontrolled case. These findings highlight the need for randomized controlled trials to determine the efficacy and safety of Cytoflavin as an adjuvant neuroprotective therapy in patients with ASE.</i> Keywords: <i>Cytoflavin, Stroke Iskemik, NIHSS, Infark Lacunar.</i>

INTRODUCTION

Stroke is an increasing cause of neurological disability and mortality worldwide and is no longer confined to older adults. In young adults, the increasing prevalence of modifiable vascular risk factors, including uncontrolled hypertension, diabetes mellitus, obesity, dyslipidemia, and smoking, has contributed to a growing burden of ischemic stroke during the productive years of life (Ekker et al., 2023; Timur et al., 2025). These risk factors may contribute to small-vessel disease and lacunar infarction through endothelial dysfunction, atherosclerotic processes, and lipohyalinosis (Qawasmeh et al., 2020; Wu et al., 2025; Yi et

al., 2021). Lacunar infarctions commonly involve the deep subcortical structures, including the basal ganglia. An important clinical problem during the acute phase is early neurological deterioration (END), characterized by worsening of pre-existing neurological deficits after initial presentation. The National Institutes of Health Stroke Scale (NIHSS) provides a standardized measure for quantifying neurological impairment and monitoring changes over time. In clinical research, END has commonly been operationalized as an increase in NIHSS score of ≥ 4 points within the first 24–72 hours after stroke onset or initial assessment, although definitions vary across studies (Duan et al., 2025a; Qawasmeh et al., 2020). Progressive deterioration of neurological function is clinically relevant because it may indicate extension of ischemic injury or other complications during the early phase of stroke.

Acute ischemic stroke is primarily managed through timely reperfusion when indicated, antithrombotic therapy, physiological support, secondary prevention, and rehabilitation. However, the persistence of ischemic tissue injury despite restoration or maintenance of cerebral perfusion has prompted investigation of adjunctive metabolic and neuroprotective strategies (Duan et al., 2025a; Ekker et al., 2023; Ermine et al., 2021; Herpich & Rincon, 2020; Powers, 2020). Cytoflavin is a metabolic formulation containing succinic acid, riboflavin, inosine, and nicotinamide. Its proposed neuroprotective effects are related to modulation of mitochondrial energy metabolism, enhancement of oxidative phosphorylation, support of ATP production, and reduction of metabolic consequences of hypoxia and oxidative stress. Preclinical studies have reported that components of Cytoflavin may support cellular energy metabolism and increase tissue tolerance to ischemic or hypoxic conditions. Clinical studies in patients with ischemic stroke have also reported potential improvements in neurological recovery and functional outcomes when Cytoflavin is administered as an adjunct to conventional treatment. However, the available clinical evidence remains heterogeneous, with limitations in study design, sample size, and methodological rigor, and robust randomized evidence establishing its efficacy in acute stroke remains limited. Therefore, observations from individual cases should be considered hypothesis-generating rather than evidence of treatment efficacy.

Acute Stroke in Evolution (ASE) represents a clinical presentation in which neurological deficits worsen during the early phase of ischemic stroke. In the literature, the related term early neurological deterioration (END) has been used to describe measurable worsening after initial assessment, with an increase in NIHSS of ≥ 4 points within the first 72 hours being one commonly used operational definition (Duan et al., 2025a). END may occur in patients with lacunar infarction and can complicate the clinical course despite initial

management. Serial NIHSS assessment is therefore useful for documenting the temporal trajectory of neurological deficits and identifying changes during the acute phase. In this context, documenting the clinical course of patients with ASE who receive adjunctive metabolic therapy may provide preliminary observations for further investigation.

The present case involves a 38-year-old man with a lacunar ischemic stroke involving the left basal ganglia and multiple uncontrolled vascular risk factors. The patient developed neurological deterioration during the acute phase, demonstrated by a marked increase in NIHSS score, followed by neurological improvement during treatment with Cytoflavin as an adjunct to comprehensive stroke management. To our knowledge, no case report has serially documented NIHSS changes in a young adult with lacunar ischemic stroke presenting with ASE who received Cytoflavin as adjunctive therapy. This case is therefore presented as a hypothesis-generating observation to describe the temporal clinical course and neurological changes during treatment, while recognizing that a single uncontrolled case cannot establish a causal relationship between Cytoflavin and neurological recovery. The findings may help inform the design of future controlled studies evaluating the potential role and safety of Cytoflavin in patients with ASE.

METHODS

This was a prospective, single-case observational report conducted in the neurology ward of Dr. Chasbullah Abdul Majid Regional Hospital, Bekasi City. The observation period extended from hospital admission (day 0) to day 10. This case was selected because it involved a young adult with lacunar ischemic stroke, multiple uncontrolled vascular risk factors, and documented neurological deterioration, with complete serial NIHSS assessments. The patient was a 38-year-old man with sudden right-sided weakness, dysarthria, and facial deviation. Diagnosis was based on clinical findings and non-contrast head CT showing a left basal ganglia lacunar infarction. Neurological status was assessed using the National Institutes of Health Stroke Scale (NIHSS). The same standardized NIHSS criteria were used at each assessment to ensure consistency. Motor strength was assessed using the Medical Research Council (MRC) scale, together with cranial nerve and speech examinations. Cytoflavin 500 mg diluted in 100 mL of 0.9% sodium chloride was administered intravenously three times daily for 10 days. Concomitant treatment included antiplatelet therapy, statin therapy, antihypertensive therapy, and glycaemic control according to the treating physician's regimen.

Clinical data were collected prospectively through direct observation, patient/family interviews, medical records, laboratory investigations, and imaging. The primary outcome was

the serial change in NIHSS score from admission through neurological deterioration and day 10. Secondary outcomes included changes in motor strength, speech, cranial nerve findings, and treatment-related adverse events. Data were analyzed descriptively and presented chronologically. No causal inference regarding Cytoflavin efficacy was made because this was a single uncontrolled case. This report has been reviewed in advance by the ethics committee of the Institute for Research and Community Service (LPPM) UKI, under number 055/UKI.LPPM/PPM.00.00/ET.2024.

RESULTS

Patient Characteristics

A 38-year-old male patient presented with sudden-onset right-sided limb weakness, slurred speech, and facial drooping approximately 12 hours before admission. The patient had several documented vascular risk factors, including uncontrolled hypertension, type 2 diabetes mellitus, obesity, dyslipidemia, and active smoking. Neurological examination revealed central paresis of cranial nerves VII and XII, right-sided hemiparesis, and motor strength of 4/5 in both the right upper and lower extremities according to the Medical Research Council (MRC) scale. The initial National Institutes of Health Stroke Scale (NIHSS) score was 5, indicating a mild neurological deficit.

Neuroimaging Findings

A non-contrast head computed tomography (CT) scan performed on admission demonstrated a small, well-defined hypodense lesion localized in the left basal ganglia, consistent with a lacunar infarction (Figure 1). There was no evidence of intracranial hemorrhage, mass effect, or perilesional edema. The lateral ventricles were not dilated, and the midline structures remained centered.

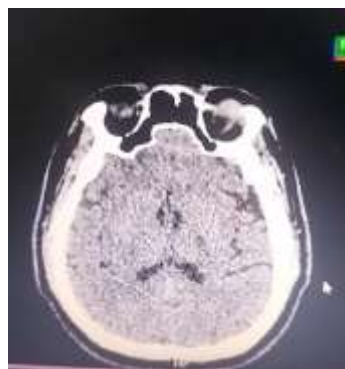


Figure 1. CT scan of the head showing a lacunar infarction of the left basal ganglia

Early Neurological Deterioration (Day 4)

On hospital day 4, the patient developed neurological deterioration. Upon awakening, he reported increased heaviness and weakness of the right upper and lower extremities accompanied by worsening speech difficulty. Neurological examination demonstrated mild aphasia and a reduction in motor strength to 2/5 in both the right upper and lower extremities. The NIHSS score increased from 5 on admission to 12 on day 4.

Following this deterioration, intravenous cytoflavin therapy was initiated at a dose of 500 mg diluted in 100 mL of sodium chloride solution and administered three times daily. Serial Response to Therapy Neurological status was assessed serially according to the assessment schedule specified in the Methods. The clinical course is summarized in Figure 2. During the initial period following neurological deterioration, no significant clinical improvement was observed. By day 6, speech had become clearer, aphasia had improved, and motor strength in the right upper and lower extremities had increased to 3/5.

By day 10, further neurological improvement was observed. The patient was able to ambulate, with motor strength of 5-/5 in the right upper and lower extremities, indicating only mild residual hemiparesis. Mild dysarthria and mild paresis of cranial nerves VII and XII persisted. The NIHSS score decreased to 4.

Cytoflavin was administered for 10 days beginning on day 4, corresponding to treatment through day 13. The final neurological assessment reported in this case was performed on day 10

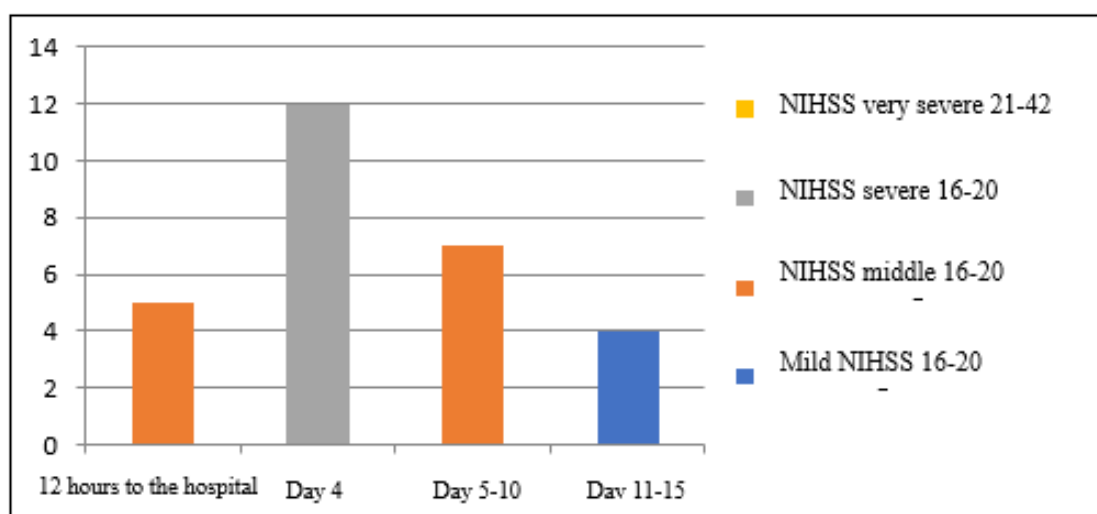


Figure 2. Comparison diagram of NIHSS from day 1 to 15 in ischemic stroke patients given Cytoflavin therapy

DISCUSSION

Lacunar Stroke, Multiple Risk Factors, and Early Neurological Deterioration

Lacunar infarction is commonly related to cerebral small-vessel disease and is strongly associated with vascular risk factors such as hypertension and diabetes mellitus. In this patient, the coexistence of five major vascular risk factors at a relatively young age provides a clinically important context for the development of small-vessel ischemic stroke. Chronic hypertension can contribute to structural changes in penetrating arterioles, including lipohyalinosis and arteriolar wall degeneration, while diabetes mellitus and dyslipidemia promote endothelial dysfunction and microvascular injury. Smoking and obesity may further contribute to vascular inflammation and metabolic dysfunction. The combination of these factors may therefore contribute to the development and progression of lacunar ischemic injury.

The occurrence of END is particularly relevant to this case. END is recognized in acute lacunar stroke despite the frequently mild neurological deficit at presentation. A recent systematic review involving more than 13,000 participants reported a pooled END incidence of approximately 23.5%, although substantial heterogeneity existed between studies. Hypertension, diabetes, and smoking were among the factors associated with END, and most studies reporting functional outcomes found that END was associated with poorer subsequent outcomes (Duan et al., 2025b, 2025a; Pan et al., 2025).

The patient's increase in NIHSS from 5 to 12 represents a substantial neurological worsening. Previous observational studies have similarly demonstrated that END is associated with unfavorable functional outcomes. In one prospective cohort of MRI-defined lacunar stroke, END occurred in 16.7% of patients and was associated with reduced odds of a favorable 90-day outcome. Another study involving 638 patients with lacunar stroke reported END in 16.9% of patients, with most episodes occurring within 72 hours, and found that END was independently associated with unfavorable outcome at discharge. Higher admission systolic blood pressure was also associated with increased risk of END in that study (kurnia.ekaptiningrum, 2023).

Several mechanisms have been proposed for END in lacunar stroke, including progression of the perforating artery lesion, extension of the infarct, impaired local perfusion, and changes in collateral or microvascular flow. In the present case, the available CT findings cannot establish which of these mechanisms was responsible for the deterioration. The patient's diabetes, hypertension, and other vascular risk factors may have contributed to vulnerability to neurological worsening, but causality cannot be determined from a single case.

Neurological Recovery and the Potential Role of Cytoflavin

The patient subsequently demonstrated substantial neurological improvement. After the deterioration on day 4, Cytoflavin was initiated, and by day 6 the patient's speech had become clearer, aphasia had improved, and right-sided motor strength had increased from 2/5 to 3/5. By day 10, motor strength had improved to 5-/5, the patient was able to ambulate, and the NIHSS had decreased to 4. This sequence provides a temporal association between initiation of Cytoflavin and neurological improvement.

Previous studies have also reported potential neurological and functional benefits of Cytoflavin when administered as an adjunct to conventional treatment for acute ischemic stroke. A multicenter randomized study involving 70 patients reported reductions in neurological deficit and improvements in activities of daily living among patients receiving Cytoflavin in addition to basic therapy. Another study involving 55 patients receiving thrombolytic therapy reported greater reduction in NIHSS and better Rankin and Barthel outcomes in patients treated with Cytoflavin compared with basic treatment alone. A larger multicenter randomized trial involving 373 patients also evaluated Cytoflavin as an adjunct to standard therapy and reported differences in cerebral lesion evolution and selected neurological, functional, and cognitive outcomes (Feske, 2021; Herpich & Rincon, 2020; Powers, 2020).

These findings provide a rationale for considering Cytoflavin as a possible adjunctive metabolic intervention, but they should be interpreted cautiously. The available studies differ in patient populations, treatment regimens, concomitant therapies, outcome measures, and follow-up periods. Moreover, the evidence base does not yet provide sufficiently consistent evidence to establish Cytoflavin as a standard treatment for acute ischemic stroke. A recent systematic review and meta-analysis reported associations between Cytoflavin and improved acute stroke outcomes, but also emphasized substantial heterogeneity across the included studies. In addition, a recent phase III randomized study has evaluated Cytoflavin in post-stroke rehabilitation rather than establishing its efficacy specifically for acute neurological deterioration following lacunar stroke.

The mechanism proposed for Cytoflavin is biologically plausible but should not be interpreted as proof of clinical efficacy. Cytoflavin contains succinic acid, riboflavin, nicotinamide, and inosine and has been proposed to support cellular energy metabolism and antioxidant processes. These effects could theoretically be relevant in ischemic tissue, where mitochondrial dysfunction, oxidative stress, and impaired energy metabolism occur. Nevertheless, neurological recovery following ischemic stroke is multifactorial. Resolution of

reversible ischemic dysfunction, restoration of microvascular perfusion, stabilization of the infarct, reduction of edema, spontaneous neurological recovery, and rehabilitation may all contribute to clinical improvement.

Importantly, spontaneous recovery must be considered in interpreting this case. Neurological improvement can occur during the early phase of ischemic stroke even without a specific neuroprotective intervention. Studies of acute ischemic stroke have demonstrated substantial spontaneous improvement during the first days after stroke onset, while the relationship between early NIHSS and later functional status changes over time is complex. Therefore, the improvement observed after day 4 cannot be attributed specifically to Cytoflavin on the basis of temporal sequence alone. Standard stroke management and the natural course of recovery may have contributed substantially to the observed outcome.

The previously cited Kharitonova et al. study concerning diabetic polyneuropathy should not be used as direct evidence for Cytoflavin efficacy in acute ischemic stroke because diabetic neuropathy and acute cerebral ischemia represent different clinical conditions and outcomes. Evidence from diabetic polyneuropathy may provide information regarding the drug's effects in another metabolic neurological condition, but it does not establish efficacy in acute stroke. Therefore, it has been omitted from the evidence supporting the stroke-specific therapeutic effect in this discussion.

NIHSS and Functional Outcome

The NIHSS was used in this case to quantify the severity and temporal evolution of neurological impairment. The decrease from 12 on day 4 to 4 on day 10 indicates substantial improvement in the measured neurological deficits, particularly motor and language functions. However, NIHSS is primarily an impairment-based neurological scale and should not be considered equivalent to a comprehensive measure of functional independence (Duan et al., 2025a).

The modified Rankin Scale (mRS), particularly when assessed at 90 days, is widely used to evaluate global functional outcome after ischemic stroke. NIHSS and mRS measure related but different aspects of recovery: NIHSS primarily quantifies neurological impairment, whereas mRS evaluates the patient's overall level of disability and dependence in daily activities. Recent evidence indicates that early NIHSS measurements have meaningful but imperfect agreement with 90-day mRS outcomes, and early NIHSS can misclassify a proportion of patients with respect to later functional status.

This distinction is particularly important in the present case. Although the NIHSS decreased to 4 and the patient was able to ambulate by day 10, a 90-day mRS assessment was

not available. Consequently, the case demonstrates early neurological recovery but cannot establish the patient's long-term functional independence or disability status. Future case reporting should ideally include a standardized 90-day mRS assessment to provide a more clinically meaningful measure of functional outcome.

Clinical Implications

The case highlights two clinically relevant issues. First, a young patient with lacunar stroke may develop substantial neurological deterioration despite a relatively mild neurological deficit at presentation. Second, the subsequent improvement illustrates the complexity of interpreting recovery following END (Rahnemayan et al., 2025). The temporal relationship between Cytoflavin administration and neurological improvement is noteworthy and supports the rationale for further investigation, but it should not be interpreted as evidence of treatment efficacy.

The management of vascular risk factors remains fundamental in patients with lacunar stroke. Hypertension, diabetes, dyslipidemia, obesity, and smoking represent potentially modifiable factors that require long-term management to reduce the risk of recurrent cerebrovascular events. In a young patient with multiple uncontrolled risk factors, secondary prevention is particularly important because the cumulative exposure to vascular risk factors may contribute to recurrent stroke and progressive small-vessel disease.

Limitations

Several limitations should be considered when interpreting this case. First, this is a single-patient case, and the findings cannot be generalized to other patients with lacunar stroke or END. Second, selection bias cannot be excluded because the patient was selected for case reporting based on the clinical course and observed response. Third, the temporal improvement following Cytoflavin administration does not establish causality because there was no untreated or placebo control group, and spontaneous neurological recovery may have occurred independently of the intervention. A placebo effect or nonspecific effects of additional clinical attention also cannot be excluded.

Fourth, the treatment was not blinded, and both the treating team and the patient were aware of Cytoflavin administration. Fifth, neurological assessments were performed by a single rater, which may introduce observer-related measurement bias in NIHSS scoring. Sixth, the patient received concomitant standard stroke therapies, making it impossible to isolate the effect of Cytoflavin from the effects of antiplatelet treatment, vascular risk-factor management, supportive care, rehabilitation, and the natural course of recovery. Finally, the absence of a 90-day mRS assessment limits conclusions regarding long-term functional outcome.

Therefore, this case should be regarded as a hypothesis-generating clinical observation rather than evidence establishing the efficacy of Cytoflavin for END after lacunar ischemic stroke. Controlled, adequately powered, blinded clinical trials with prespecified functional outcomes, particularly 90-day mRS, are required to determine whether Cytoflavin provides benefit beyond standard stroke care.

CONCLUSIONS

This case study presents a young patient with lacunar stroke who experienced early neurological deterioration followed by substantial clinical improvement during comprehensive medical management. The management included acute stroke care, intensive control of vascular risk factors, and Cytoflavin as an adjuvant therapy. In this single case, Cytoflavin appeared safe and was temporally associated with rapid neurological recovery; however, its specific contribution to the observed improvement cannot be isolated from the effects of the comprehensive management package, and its efficacy requires confirmation in randomized controlled trials. Serial NIHSS assessment is essential for monitoring neurological changes and treatment response. In young patients with stroke, aggressive secondary prevention through optimal control of hypertension, diabetes mellitus, dyslipidaemia, and obesity, together with smoking cessation, is crucial to reduce the risk of recurrent cerebrovascular events. Future research should include randomized, placebo-controlled trials evaluating Cytoflavin in acute ischemic stroke, with NIHSS and 90-day modified Rankin Scale (mRS) as key clinical endpoints.

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