
Comprehensive Clinical Evaluation and Therapeutic Progression of a 70-Year-Old Female Following Ischemic Infarction: A Case Study in Integrated Pharmacotherapy and Intravenous Oxyhydrogen-Nitric Oxide Nanobubble Intervention

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Case Report

Comprehensive Clinical Evaluation and Therapeutic Progression of a 70-Year-Old Female Following Ischemic Infarction: A Case Study in Integrated Pharmacotherapy and Intravenous Oxyhydrogen-Nitric Oxide Nanobubble Intervention

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Abstract

Background: Ischemic stroke represents a catastrophic disruption of the neurovascular architecture, often resulting in permanent functional deficits due to the irreversible nature of neuronal core death and the precarious state of the surrounding penumbra. This report provides an exhaustive analysis of the clinical course and recovery of Mrs. L, a 70-year-old female patient residing in Jakarta, who suffered an ischemic stroke event characterized by left-side hemiparesis and significant mobility impairment. **Case Presentation:** The therapeutic framework employed a dual-track strategy: a conventional pharmacological regimen designed to maximize secondary prevention and neurorestorative support—utilizing citicoline, atorvastatin-ezetimibe, dual antiplatelet therapy, and antihypertensive management—and an innovative adjunctive protocol involving the intravenous administration of oxyhydrogen (HHO) nanobubbles and liquid nitric oxide (NO). The patient underwent a structured 30-session program divided into Basic and Booster phases. Quantitative assessment revealed a rapid clinical evolution from a bedrest-dependent state with severe motor weakness (muscle strength graded at 2/22 in the left extremities) to independent mobility without assistive devices within seventeen days. **Conclusions:** The synergy between these modalities suggests that integrated nanomedicine may support the recovery timeline for elderly stroke survivors, addressing both the neurological damage and the underlying metabolic instability.

Keywords: ischemic stroke; oxyhydrogen nanobubbles; nitric oxide; adjunctive therapy; functional recovery; case report

1. Introduction

Ischemic stroke is defined by an interruption of blood supply to the brain, leading to an immediate loss of neurological function that often manifests as speech deficits, cognitive reduction, and loss of muscular control [1]. Within the global healthcare landscape, stroke remains a leading cause of mortality and adult disability, with ischemic subtypes accounting for approximately 65.3% of incident stroke cases worldwide in 2021 [2]. The sudden occlusion of cerebral arteries by a blood clot or plaque initiates a complex cascade of pathological events termed the “ischemic injury cascade,” which evolves through several hemodynamic phases: hyperacute, acute, subacute, and chronic [1].

The primary hurdle in the treatment of ischemic stroke is the “time is brain” paradigm [3]. Every minute of untreated ischemia has been estimated to result in the loss of approximately 1.9 million neurons, 14 billion synapses, and 12 kilometers of myelinated fibers [3]. When blood flow is restricted, adenosine triphosphate (ATP) levels drop precipitously, leading to the failure of energy-dependent

ionic pumps. This failure triggers membrane depolarization and the excessive release of glutamate, an excitatory neurotransmitter that causes calcium (Ca²⁺) overload within the neurons [1]. This secondary intracellular calcium surge leads to oxidative stress, mitochondrial dysfunction, and the production of reactive oxygen species (ROS) that destroy cellular macromolecules, including lipids, proteins, and DNA [1].

Standard interventions, such as the administration of recombinant tissue plasminogen activator (rt-PA) and mechanical thrombectomy, are restricted by narrow therapeutic windows—generally 4.5 hours for intravenous rt-PA in eligible patients and up to 24 hours for mechanical thrombectomy in selected patients—and may be precluded by the risk of hemorrhagic transformation and other contraindications [4,5]. Even when recanalization is successful, reperfusion injury can occur as the influx of oxygen generates a surge of free radicals, further damaging the blood-brain barrier (BBB) and neurovascular unit [6]. This highlights an urgent need for neuroprotective and neurorepair strategies that can bridge the gap between acute intervention and long-term rehabilitation.

Nanotechnology has emerged as a promising frontier in overcoming the physiological barriers of the central nervous system (CNS) [1]. The blood-brain barrier is a highly selective interface that limits the entry of most therapeutic agents into the brain parenchyma [7]. Nanoparticles and nanobubbles (NBs), characterized by their ultra-small scale (typically 1 to 200 nm) [1,8], have been investigated for delivery across this barrier, with certain engineered nanoparticles shown to penetrate it through endothelial transcytosis [7,9] or by exploiting the increased permeability found in ischemic brain regions [1,7].

Molecular hydrogen (H₂), a component of oxyhydrogen (HHO) therapy, and nitric oxide (NO) donors have demonstrated preclinical potential in mitigating several pathological processes associated with ischemia [10,11]. Molecular hydrogen (H₂) can rapidly diffuse across cell membranes and has been proposed to act as a selective antioxidant against highly reactive species, such as the hydroxyl radical (•OH) and peroxynitrite (ONOO⁻) [10]. Nitric oxide, acting as a signaling molecule, regulates vascular tone, and experimental studies indicate that inhaled NO can dilate collateral arterioles in the ischemic penumbra and improve local blood flow [11,12]. This case report evaluates the synergistic application of these nanotechnological tools alongside standard pharmacotherapy in an elderly female patient, providing a nuanced understanding of how integrated medicine can optimize functional recovery and systemic metabolic health.

2. Case Presentation

2.1. Patient Information

The patient, identified as Mrs. L., is a 70-year-old female. On January 20, 2026, the patient experienced a sudden fall in her kitchen, which resulted in immediate neurological deficits. The primary presenting symptom was a profound weakness of the left extremities (hemiparesis), accompanied by sensory disturbances and an inability to maintain an upright posture for meaningful durations.

Following the acute event, the patient was admitted to Rumah Sakit Pondok Indah, where diagnostic imaging and laboratory investigations confirmed an ischemic stroke (infarct). The clinical consensus attributed the stroke to advanced hyperlipidemia, a condition characterized by high circulating levels of cholesterol which facilitates the formation of atherosclerotic plaques and eventual arterial occlusion. The patient's clinical profile was further complicated by three significant metabolic comorbidities:

1. Hyperlipidemia: Baseline labs showed a total cholesterol level of 249 mg/dL and an LDL level of 165 mg/dL, both of which are substantially above the clinical targets for a high-risk post-stroke patient.
2. Prediabetes: An HbA1c level of 5.7% was recorded, placing the patient at the threshold of diabetes mellitus and indicating a chronic state of metabolic stress that contributes to microvascular fragility.

3. Hypokalemia: A potassium level of 3.1 mmol/L (reference: 3.4 – 4.4 mmol/L) was noted, which may have exacerbated muscle weakness and affected cardiac electrical stability during the acute phase of recovery.

Prior to the stroke, the patient was active within her home environment. The transition from independence to a bedrest-dependent state following the kitchen fall posed a significant psychological and physiological burden. The patient reported constant numbness in her left side and difficulty performing any weight-bearing activities.

2.2. Clinical Findings

At the start of the therapeutic intervention on January 29, 2026, a comprehensive physical examination was conducted to establish a baseline for recovery. The patient was predominantly in a bedrest state, exhibiting a typical post-stroke motor profile.

Table 1. Baseline Muscle Strength and Functional Assessment

Assessment Category	Clinical Finding	Grading/Score
Right Side Motor Strength	Normal	555 / 555
Left Side Motor Strength	Severe Weakness	222 / 222
Gait/Ambulation	Non-ambulatory	Requires full assistance
Posture Control	Weak	Unable to stand upright long
Pain Level (Back)	Scale 3 (Soreness)	Present during sitting
Sensory Function	Numbness	Localized to left side

Grading Note: 555 represents normal strength; 222 represents the ability to move the limb but an inability to resist gravity.

The laboratory findings from January 20 to 22, 2026, emphasize the systemic metabolic imbalance that likely triggered the ischemic event and hindered early recovery.

Table 2. Initial Metabolic and Electrolyte Panel.

Biomarker	Patient Value	Reference Range	Status
Total Cholesterol	249 mg/dL	< 200 mg/dL	High
LDL Cholesterol	165 mg/dL	< 130 mg/dL	High
HbA1c	5.7 %	4.0 - 5.6 %	Prediabetes
Potassium (K+)	3.1 mmol/L	3.4 - 4.4 mmol/L	Low

The identification of hyperlipidemia as the primary cause of the stroke underscores the necessity for aggressive lipid management in conjunction with neurological repair.

2.3. Timeline

The patient's recovery followed a structured timeline, beginning with the diagnostic and stabilization phase in a hospital setting, followed by an intensive two-phase nanobubble program.

Table 3. Clinical Progression and Therapeutic Milestones.

Date	Milestone	Clinical Status & Observations
Jan 20, 2026	Acute Event	Fall in kitchen; stroke diagnosis at Pondok Indah Hospital.
Jan 20-22, 2026	Labs/Baseline	High LDL and prediabetes identified; bedrest initiated.
Jan 29, 2026	Start of Package I	1st NB Infusion; Muscle strength 555/222; Left-side weakness.
Feb 01, 2026	Progression	3rd NB Infusion; Subjective feeling of "freshness" and energy.
Feb 08, 2026	Progression	6th NB Infusion; Patient begins walking with a quadripod cane.
Feb 11, 2026	Progression	7th NB Infusion; Improvement in standing duration and leg power.
Feb 15, 2026	Functional Jump	9th NB Infusion; Patient walks independently without a cane.
Feb 20, 2026	Progression	13th NB Infusion; Increased confidence; Walking is stable.
Feb 23, 2026	End of Package I	Completion of 15 Basic infusions; Significant mobility gains.
Mar 09, 2026	Start of Package II	Commenced 15x Booster infusions; Focus on metabolic stability.
Present	Current State	Ongoing therapy; Sustained independent ambulation.

2.4. Therapeutic Intervention

The therapeutic approach for Mrs. L was multi-layered, integrating the pharmacological standards of modern neurology with the emerging capabilities of nanobubble-based gas therapy.

2.4.1. Standard Pharmacological Management

To address the risk of recurrent ischemia and manage her chronic comorbidities, the patient was prescribed several medications. Citicoline (Brainact) 500 mg was administered as a neuroprotective agent. Atorvastatin/ezetimibe (Atozet) 10/40 mg was administered as a lipid-lowering combination. Clopidogrel (Plavix) 75 mg and aspirin (Cardio Aspirin) 100 mg were administered as dual antiplatelet therapy to prevent thrombus formation on atherosclerotic plaques. Pantoprazole (Vomizole) 20 mg was provided for gastric protection to mitigate the risk of gastrointestinal bleeding associated with aspirin use. Telmisartan/amlodipine (Twynsta) 40/5 mg was administered as a dual-mechanism antihypertensive treatment to maintain blood pressure within a clinically appropriate range.

2.4.2. Nanobubble and Gas Therapy

The patient received intravenous therapeutic gases using nanobubble technology as part of a specialized treatment program.

1. Oxyhydrogen Nanobubbles (NB-HHO)

Oxyhydrogen (HHO) is a gaseous mixture of two parts hydrogen and one part oxygen. In this protocol, these gases are encapsulated in nanoscale bubbles (10-200 nm in diameter) suspended in

500 mL of normal saline. The treatment followed a dose-escalation schedule. Infusions began at a volume of 5 mL and were gradually increased by 5 ml increments in subsequent sessions, reaching a maximum dose of 50 ml per session. Nanobubbles exhibit high internal pressure and a large surface area, allowing them to remain stable in liquid media for days to months, far outlasting conventional microbubbles [8].

2. Nitric Oxide

A dose of 2.5 ml of liquid nitric oxide was administered alongside the HHO infusion. This component serves as a potent vasodilator and signaling molecule designed to optimize the microcirculatory environment for the uptake of the oxyhydrogen payload [11,12].

3. Therapeutic Structure

The program was divided into two phases. The Basic Phase comprised 15 sessions, conducted from January 29 to February 23, 2026. This phase targeted the subacute recovery window, aiming to reduce neuroinflammation and promote the early "waking" of the penumbra. The Booster Phase comprised an additional 15 sessions and commenced on March 9, 2026. This phase was intended to consolidate motor gains, support neurogenesis, and address systemic metabolic markers (cholesterol and blood sugar stability).

2.5. Follow-Up and Outcomes

The functional outcomes for Mrs. L were assessed through subjective reports and observed motor milestones during the 30-session program.

2.5.1. Functional Mobility Progression

The most remarkable clinical finding was the speed at which the patient regained independent ambulation.

Table 4. Comparative Mobility Status Over Therapy.

Milestone	Timeframe (Days)	Device/Support Used	Subjective Status
Baseline	Day 0	Bedrest	Left weakness, numbness
Package I, Infusion 3	Day 4	Bedrest / Sitting	Feels "fresh" and energized
Package I, Infusion 6	Day 11	Quadripod (Tripod) Walker	Can stand and walk short distance
Package I, Infusion 9	Day 17	None (Independent)	Walks without a cane
End of Package I	Day 25	Independent	Confident walking, stable gait

The transition from a 222 strength (unable to resist gravity) to independent walking in seventeen days is significantly faster than the typical rehabilitation trajectory for a 70-year-old stroke patient.

2.5.2. Symptom Resolution and Quality of Life

The initial lower back pain (grade 3), which the patient experienced while sitting, resolved completely (grade 0) by the middle of Package I. This is likely due to the systemic anti-inflammatory effects of the HHO therapy and improved core muscle recruitment as motor function returned. The patient consistently reported feeling fresher and more energetic. This suggests an improvement in mitochondrial efficiency and a reduction in post-stroke fatigue, which is often a barrier to physical therapy. The patient noted a gradual reduction in the numbness of her left limbs, indicating recovery of the somatosensory pathways.

2.5.3. Long-Term Stabilization

During the Booster phase, the patient maintained her independent mobility and reported continued stamina. No adverse events, such as headaches, hypertension spikes, or localized infusion reactions, were observed throughout the 30-session course. The laboratory re-evaluation is scheduled to monitor the impact of the therapy on LDL cholesterol and HbA1c levels.

3. Discussion

3.1. Biological Mechanisms of Oxygen-Delivering Nanobubbles (ODNBs) in Stroke

The use of oxygen-delivering nanobubbles (ODNBs) in Mrs. L's case addresses the primary physiological deficit in ischemic stroke: cerebral hypoxia [1,13]. In many stroke cases, even after the primary clot is dissolved or removed, the microvasculature in the penumbra remains poorly perfused due to edema, leukocyte plugging, and pericyte constriction—a state known as the “no-reflow” phenomenon [14]. Standard oxygen therapy increases the dissolved oxygen in the blood, but this oxygen may not reach the deep tissue of the penumbra if blood flow is mechanically restricted [14,15]. Nanobubbles, however, are small enough to pass through constricted capillaries and reach oxygen-deprived brain regions [13,16]. Once in a hypoxic environment, the concentration gradient triggers a controlled release of oxygen directly to the neurons [16].

The penumbra is composed of “functionally silent” neurons that have ceased signaling to conserve energy but have not yet undergone necrosis [17]. By providing an immediate and targeted supply of oxygen, nanobubbles can restore mitochondrial ATP production in these cells, allowing them to resume signaling and regain motor control [13,16]. This mechanism likely explains the rapid improvement in Mrs. L's muscle strength and gait within the first two weeks of therapy.

3.2. Molecular Hydrogen (H₂) as a Selective Neuroprotectant

The hydrogen component of HHO therapy provides a unique antioxidant advantage that traditional pharmacological agents lack [10]. Traditional antioxidants, such as Vitamin E or C, are often ineffective in stroke trials because they indiscriminately neutralize all ROS, including beneficial signaling molecules like hydrogen peroxide (H₂O₂) [10]. Molecular hydrogen is a “smart” antioxidant; it selectively reacts with the hydroxyl radical (•OH) and peroxynitrite (ONOO⁻), the most destructive species that cause irreversible cellular damage [10]. By neutralizing these radicals, H₂ protects the vascular endothelium and the neuronal membranes, effectively preventing the “second hit” of damage that typically follows an initial ischemic event [6,10].

The acute and subacute phases of stroke are dominated by neuroinflammation, where microglia (the brain's resident macrophages) transform into a pro-inflammatory M1 phenotype, releasing cytokines such as TNF-α and IL-1β [1,6]. These cytokines further disrupt the BBB by upregulating matrix metalloproteinases (MMPs), particularly MMP-9, which degrades the basement membrane [6]. Molecular hydrogen has been shown to suppress the expression of these pro-inflammatory cytokines and inhibit MMP-9 activity [10,18]. This reduction in inflammation preserves the integrity of the BBB and prevents the formation of cerebral edema, which was critical for Mrs. L's ability to transition from bedrest to sitting and standing without pain [6,18].

3.3. Nitric Oxide (NO) and Vascular Restoration

The inclusion of liquid nitric oxide in the protocol provides essential support for vascular hemostasis and lipid management [11,19]. In the hyperacute and acute stages, the brain attempts to compensate for a blockage by opening collateral vessels [12]. Nitric oxide is the primary endogenous signaling molecule that facilitates this vasodilation [11]. Exogenous NO supplementation can improve the perfusion of the ischemic penumbra by dilating these collateral channels [12]. Furthermore, NO inhibits platelet aggregation and prevents leukocytes from adhering to the vessel walls, thereby reducing the risk of further microthrombi [11].

A critical etiological factor in Mrs. L's case was her high LDL cholesterol (165 mg/dL). Emerging research indicates a profound link between nitric oxide and lipid metabolism [19]. Nitric oxide has been found to inhibit PCSK9 (Proprotein Convertase Subtilisin/Kexin type 9), an enzyme that degrades LDL receptors on the liver [19]. By inhibiting PCSK9, NO increases the number of available LDL receptors, facilitating the more efficient clearance of “bad” cholesterol from the bloodstream [19]. This systemic effect likely works in synergy with the patient's Atozet medication to stabilize her lipid profile and reduce the risk of a recurrent stroke.

3.4. Nanobubble Stability and BBB Crossing Mechanisms

The proposed efficacy of Mrs. L's treatment would be dependent on the ability of the HHO nanobubbles to maintain their integrity and enter the brain parenchyma [8,16]. Research into HHO and H₂ nanobubbles shows that H₂ nanobubbles are most stable at a neutral pH (6–7) [8]. They can be sensitive to extreme heat [8]. This stability could allow the bubbles to circulate long enough to encounter the cerebral vasculature.

Nanoparticles and nanobubbles have been investigated for entering the brain through several pathways [1,7,9,13]. Small, lipid-based or protein-coated nanoparticles can be internalized by endothelial cells through endocytosis or transcytosis [7,9]. During the acute and subacute phases, the BBB is naturally “leakier” due to inflammatory processes, including the upregulation of adhesion molecules such as VCAM-1 and ICAM-1 [1,6]. This “inflammatory window” allows larger payloads to accumulate at the site of injury [1,7]. In some protocols, external ultrasound is used to facilitate nanobubble-mediated delivery; however, even without ultrasound, certain engineered nanocarriers may accumulate through the hyper-permeable vasculature of the injured neurovascular unit [1,7,13,16].

3.5. Integrated Recovery: Comparing Standard and Nanomedicine

Mrs. L's recovery represents a fusion of traditional and modern medical paradigms. The combination of these elements addresses the stroke not merely as a focal brain injury, but as a systemic metabolic event [20]. The reported “Refreshed” effect is consistent with a study showing that hydrogen-rich saline improves mitochondrial membrane potential and ATP content, effectively providing a “recharge” to cellular energy systems [21].

Table 5. Synergistic Effects of Therapy Components.

Component	Primary Target	Therapeutic Synergy
Citicoline	Neuronal Membrane	Structural repair of damaged cells
Statins (Atozet)	Liver/Gut	Long-term reduction of LDL levels
H ₂ (HHO-NB)	Hydroxyl Radicals	Protects cells from reperfusion injury
O ₂ (HHO-NB)	Mitochondria	Reverses penumbral metabolic crisis
NO (Liquid)	Vasculature	Dilates collaterals and reduces LDL via PCSK9

3.6. Safety and Translational Challenges

While Mrs. L's outcomes are profoundly positive, the clinical application of nanomedicine must be approached with caution. Some inorganic nanoparticles, such as silica or titanium dioxide, can activate the inflammasome or exhibit toxicity if not properly biocoated with biocompatible materials like PEG (polyethylene glycol) or dextran [1,7]. However, gas-core nanobubbles like HHO are inherently safer because the gas eventually dissolves into the bloodstream or is exhaled, leaving no toxic metallic residues [8,10,13]. The dose-escalation strategy used for Mrs. L (5ml to 50ml) is a prudent clinical approach to monitor for potential barotrauma or hyperoxic sensitivity [13,15].

5. Conclusions

The clinical journey of Mrs. L serves as a compelling proof-of-concept for the integration of nanotechnology into the standard of care for ischemic stroke. A 70-year-old patient with hyperlipidemia and prediabetes who presents with 222 muscle strength would typically face a long, arduous recovery involving months of institutional rehabilitation. Instead, through the application of a multimodal regimen—combining intensive lipid management and neuroprotection with the intravenous delivery of selective antioxidants and therapeutic gases—the patient achieved independent ambulation in just over two weeks.

The analysis of this case suggests several key takeaways for professional peers. First, nanobubbles effectively circumvent the BBB and microvascular occlusions, providing a delivery system that can target the "inflammatory penumbra". Second, oxyhydrogen (HHO) provides a dual-action benefit: oxygen restores mitochondrial energy production in silent neurons, while hydrogen prevents the oxidative surge of reperfusion injury. Third, nitric oxide (NO) plays a systemic role beyond vasodilation, potentially aiding in the long-term management of hyperlipidemia through PCSK9 inhibition. Finally, integrated titration of these gases appears safe and well-tolerated in an elderly population, provided standard pharmacotherapy for blood pressure and thrombosis is maintained.

While this single-case success is significant, it underscores the need for broader investigative efforts. Future research should focus on quantifying the specific impact of HHO nanobubbles on post-stroke neurogenesis markers (such as VEGF and BDNF) and conducting longitudinal studies to determine if these gains in motor function are accompanied by long-term metabolic stabilization of cholesterol and blood sugar levels. For now, the synergistic recovery of Mrs. L offers a hopeful paradigm for the future of neurovascular medicine.

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Institutional Review Board Statement: The preparation and publication of this retrospective single-patient case report were conducted in accordance with the Declaration of Helsinki. Ethical review and approval were not required because the report was based solely on information documented during routine clinical care. No intervention was prospectively assigned for research purposes, and no additional procedures were performed solely for the preparation of this manuscript.

Informed Consent Statement: Written informed consent was obtained from the patient for publication of this paper and the anonymized clinical information contained herein.

Data Availability Statement: Relevant data supporting this case report are presented within the manuscript. Additional patient-level clinical records are not publicly available because of patient privacy and confidentiality restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ATP	Adenosine triphosphate
BBB	Blood–brain barrier
BDNF	Brain-derived neurotrophic factor
CNS	Central nervous system
DNA	Deoxyribonucleic acid
H ₂	Molecular hydrogen
H ₂ O ₂	Hydrogen peroxide

HbA1c	Hemoglobin A1c
HHO	Oxyhydrogen
HHO-NB	Oxyhydrogen nanobubble
ICAM-1	Intercellular adhesion molecule 1
IL-1β	Interleukin-1 beta
LDL	Low-density lipoprotein
MMP	Matrix metalloproteinase
MMP-9	Matrix metalloproteinase 9
NB	Nanobubble
NO	Nitric oxide
O ₂	Molecular oxygen
ODNB	Oxygen-delivering nanobubble
ONOO ⁻	Peroxynitrite
PCSK9	Proprotein convertase subtilisin/kexin type 9
PEG	Polyethylene glycol
ROS	Reactive oxygen species
rt-PA	Recombinant tissue plasminogen activator
TNF-α	Tumor necrosis factor alpha
VCAM-1	Vascular cell adhesion molecule 1
VEGF	Vascular endothelial growth factor
•OH	Hydroxyl radical

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