Efficacy and Safety of CT-guided Ozone Neurolysis of the Gasserian Ganglion for Idiopathic Trigeminal Neuralgia in Elderly Patients (≥70 Years Old) - A Retrospective Observational Cohort Study

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Abstract

Objective: To retrospectively analyze the long-term efficacy, safety, and durability of CT-guided ozone neurolysis of the Gasserian Ganglion in elderly patients (≥70 years old) with Idiopathic Trigeminal Neuralgia (ITN). Methods: This was a retrospective, single-center, observational cohort study. Consecutive elderly patients with ITN meeting the inclusion criteria between January 2020 and December 2022 were enrolled. All patients underwent percutaneous puncture of the foramen ovale under CT guidance, followed by injection of 5 mL of a medical-grade ozone-oxygen mixture (concentration: 30 μg/mL) around the Gasserian Ganglion. The primary efficacy endpoint was the change in pain intensity assessed using the Visual Analog Scale (VAS). Secondary endpoints included the Barrow Neurological Institute (BNI) pain intensity score, pain recurrence rate, and patient satisfaction. All perioperative and postoperative complications were systematically recorded. All patients completed a 24-month follow-up period. Results: A total of 85 patients (mean age 76.5±4.2 years) were included. The mean VAS score significantly decreased from 8.2±0.9 at baseline to 2.1±1.5 at 24 months ($P<0.001$). At the final 24-month follow-up, 69 patients (81.2%) achieved satisfactory pain control (BNI grades I-III), among whom 55 patients (64.7%) were completely pain-free without medication (BNI grade I). Kaplan-Meier survival analysis estimated the recurrence-free survival rates at 12 and 24 months postoperatively to be 85.3% and 78.5%, respectively. The most common complication was transient facial hypesthesia (10 cases, 11.8%), which resolved spontaneously within 24 hours in all instances. No instances of anesthesia dolorosa, keratitis, intracranial hemorrhage, or other serious, permanent complications occurred. Conclusion: CT-guided ozone neurolysis of the Gasserian Ganglion is a safe, effective, and durable minimally invasive method for treating elderly patients with ITN. Its non-neurodestructive nature, excellent safety profile, and repeatability offer a highly valuable therapeutic option for this special patient population, who often have multiple comorbidities and are poor candidates for traditional craniotomy or neuroablative procedures.

Keywords

Idiopathic Trigeminal Neuralgia, Ozone therapy, Age, CT guidance, Retrospective studies, Gasserian Ganglion

Introduction

Idiopathic Trigeminal Neuralgia (ITN) is a neuropathic pain syndrome characterized by brief, paroxysmal, electric shock-like pain within the distribution of the trigeminal nerve, significantly impairing patients' quality of life, with a particular predilection for the elderly population [1-3]. This excruciating pain disrupts fundamental activities, such as eating and speaking, and frequently triggers anxiety and depression, imposing a substantial health burden [4,5].

The management of ITN in elderly patients presents a clinical dilemma. First-line pharmacological agents (e.g., carbamazepine) are often poorly tolerated in the elderly due to significant central nervous system side effects (e.g., dizziness, ataxia), frequently leading to treatment failure [6-8]. For patient's refractory to medication, microvascular decompression (MVD), while considered the "gold standard" therapy, carries significantly increased perioperative risks of serious complications

(e.g., stroke, death) in the elderly as an open cranial procedure. This deters many patients with underlying comorbidities from undergoing MVD [9,10]. Alternative percutaneous neuroablative procedures (e.g., radiofrequency thermocoagulation [RFT], percutaneous balloon compression [PBC]) achieve pain relief by intenti-onally damaging the nerve conduction pathways. Consequently, they are universally associated with a high incidence of functional sequelae, primarily facial numbness and dysesthesia. Some patients even find the resultant numbness more intolerable than the original pain [11-13].

In recent years, medical ozone therapy has emerged as a novel non-neurodestructive technique, demonstrating unique potential [14]. Its mechanism of action does not involve direct destruction of neural tissue; instead, it exerts analgesic effects through potent anti-inflammatory and immune-modulatory functions. Studies indicate that medical ozone can significantly reduce local inflammatory cytokine levels by activating the Nrf_2 antioxidant pathway and inhibiting the NF-κB pro-inflammatory pathway, thereby improving the microenvironment around the nerve root and alleviating neuropathic pain [15]. This biological modulatory mechanism suggests that ozone therapy may provide effective analgesia while maximally preserving neurological function. Furthermore, as it does not cause permanent structural damage, the procedure can be safely repeated in cases of pain recurrence [16].

Although preliminary studies have reported the efficacy of ozone injections for Trigeminal Neuralgia, there remains a lack of prospective, long-term follow-up data specifically focused on the elderly, a particularly special and vulnerable population [17,18]. Therefore, this study aims to systematically evaluate the long-term efficacy, safety, and durability of CT-guided ozone neurolysis of the Gasserian Ganglion for treating elderly ITN patients aged 70 years and older, through a retrospective cohort study. We hope this will provide new evidence-based medical evidence to address the therapeutic challenges faced by this population.

Methods

Study design and ethics

This study was a retrospective, single-center, observational cohort study conducted in the Department of Pain Medicine at the Affiliated Hospital of North Sichuan Medical College between January 2020 and December 2023. The study protocol was approved by the Institutional Review Board (IRB) of our hospital. All participants provided written informed consent after being fully informed about the study details prior to enrollment. This study adhered to the ethical principles outlined in the Declaration of Helsinki.

Study participants

Patients were identified through the electronic medical record system of the Department of Pain Medicine at the Affiliated Hospital of North Sichuan Medical College. All included patients were diagnosed and treated between January 2020 and December 2022.

(1) Inclusion criteria

a) Age ≥70 years old.

b) Diagnosis of Idiopathic Trigeminal Neuralgia (ITN) fulfilling the diagnostic criteria of the International Classification of Headache Disorders, 3rd edition (ICHD-3), characterized by typical paroxysmal pain or paroxysmal pain superimposed on persistent background pain.

c) Inadequate pain relief after adequate dose and duration trials of at least two first-line medications (e.g., carbamazepine, oxcarbazepine) or discontinu-ation due to intolerable side effects.

d) Mean pre-procedure pain intensity score ≥4 (on a 0-10 scale) assessed by the Visual Analog Scale (VAS) during the week prior to treatment.

e) Deemed unsuitable candidates for microvascular decompression (MVD) due to multiple medical comorbidities, high anesthetic risk, or patient refusal to undergo craniotomy.

f) Ability to understand and provide written informed consent and cooperate with follow-up assessments.

(2) Exclusion criteria

a) Secondary Trigeminal Neuralgia caused by intracranial tumors, multiple sclerosis, or other structural lesions.

b) Active local infection at the puncture site or systemic infection.

c) Severe coagulation disorders or ongoing anticoagulant therapy that could not be safely interrupted.

d) Known allergy to ozone, local anesthetics, or contrast agents.

e) Major systemic contraindications to ozone therapy (e.g., hyperthyroidism, glucose-6-phosphate dehydrogenase [G6PD] deficiency, acute myocardial infarction,

pregnancy).

f) Severe psychiatric illness impairing pain assessment or compliance with follow-up.

Interventional procedure: CT-guided ozone neurolysis of the Gasserian Ganglion

All procedures were performed by the same experienced interventional pain physician.

(1) Patient preparation and positioning

The patient was placed in the supine position with the neck extended approximately 20° and comfortably positioned on the CT scanner table (Philips MX-16). Standard monitoring, including electrocardiography (ECG), non-invasive blood pressure (NIBP), and Saturation of Peripheral Oxygen (SpO_2), was established. Peripheral intravenous (IV) access was secured.

(2) CT scanning and trajectory planning

An initial axial thin-slice (1 mm) non-contrast CT scan of the skull base was performed to clearly delineate the anatomical structure of the ipsilateral foramen ovale. Using the CT workstation, the optimal needle trajectory was planned to utilize the infrazygomatic transcutaneous approach (Hartel's approach). The skin entry point (typically located 2-3 cm lateral to the oral commissure) was identified, and the precise puncture angle and depth were calculated to ensure the needle tip would reach the posteromedial margin of the foramen ovale. The key advantage of CT guidance is its ability to perform 3D reconstructions, providing clear visualization of vascular, neural, and bony structures. This facilitates planning a safe trajectory that avoids critical structures such as the maxillary artery, offering superior precision compared to traditional C-arm fluoroscopy guidance.

(3) Puncture and needle tip confirmation

Following standard skin disinfection and draping, local infiltration anesthesia was administered at the puncture site using 1% lidocaine. Under intermittent CT guidance, a 22-gauge, 10-cm long coaxial cannula needle (Tuoren, China) was slowly advanced along the predetermined trajectory. Serial CT images confirmed the needle tip's position upon reaching and entering the foramen ovale into Meckel's cave, the location of the Gasserian Ganglion. Neurophysiological motor/sensory testing (eliciting paresthesia or pain reproduction in the distribution of the affected trigeminal nerve branch) was performed to further confirm accurate needle placement.

(4) Ozone injection

The needle stylet was removed, and aspiration was performed to confirm the absence of blood or cerebrospinal fluid (CSF). A medical-grade ozone-oxygen mixture was freshly generated using an ozone therapy device (Ozomed Basic, Germany). A 5 mL volume of the ozone-oxygen mixture at a concentration of 30 μg/mL was injected slowly and fractionally over 60 seconds into the periganglionic space surrounding the Gasserian Ganglion. A post-injection CT scan was performed to visualize the diffusion pattern of the gas within Meckel's cave, ensuring adequate coverage of the ganglion (see Figure 1).

(5) Post-procedural management

The needle was withdrawn. The puncture site was covered with a sterile dressing and manually compressed for several minutes. The patient was transferred to the recovery room and observed in the supine position (without a pillow) for at least 2 hours. Patients were discharged the following day once vital signs remained stable.

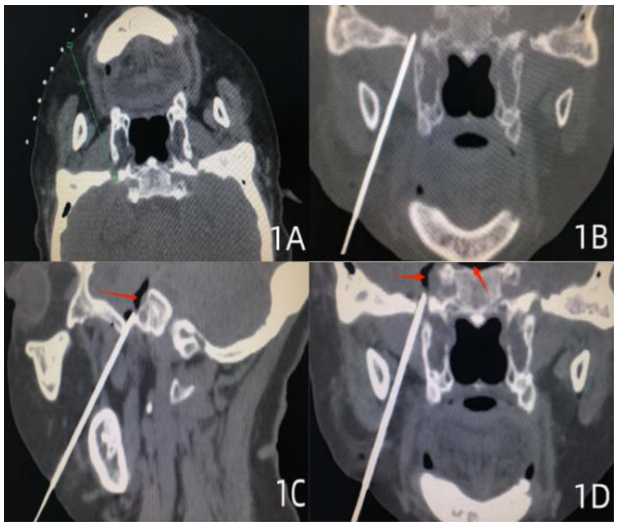

Figure 1. CT-guided ozone neurolysis of the Gasserian Ganglion.

Note: 1A: Schematic illustration of patient positioning and needle trajectory utilizing the Hartel approach. 1B: Oblique coronal CT image demonstrating the needle tip positioned within the foramen ovale. 1C-1D: Post-injection oblique sagittal (1C) and oblique coronal (1D) CT images showing diffusion of the ozone-oxygen gas mixture (appearing as hypodense gas) along the dural sheath into Meckel's cave (red arrows), confirming periganglionic distribution.

Outcome measures and follow-up

(1) Primary efficacy outcome

Change in pain intensity: Assessed using the Visual Analog Scale (VAS). The VAS is a 10-cm horizontal line

where 0 represents “no pain” and 10 represents “the worst pain imaginable”. VAS scores were recorded at baseline and all scheduled follow-up time points [19].

(2) Secondary efficacy outcomes

a) Barrow Neurological Institute (BNI) Pain Intensity Score: This five-grade scale comprehensively evaluates neurological dysfunction and medication usage, providing a more holistic assessment of clinical efficacy [20].

Grade I: No pain, no medication required.

Grade II: Occasional pain, no medication required.

Grade III: Some pain, adequately controlled with medication.

Grade IV: Some pain, not adequately controlled with medication.

Grade V: Severe pain or no relief.

Treatment success was defined as achieving a BNI pain intensity score of I, II, or III.

b) Pain recurrence: Defined as the worsening of pain requiring additional analgesic intervention or a deterioration in BNI pain intensity score to grade IV or V, occurring after an initial successful pain relief response (BNI grade I-III). The time to recurrence was recorded.

(3) Safety outcomes

a) Complications: All procedure-related intraoperative and postoperative adverse events were systematically documented.

b) Degree of Facial Numbness: Quantified using the BNI Facial Numbness Score:

Grade I: No facial numbness.

Grade II: Mild facial numbness, not bothersome.

Grade III: Facial numbness, somewhat bothersome.

Grade IV: Facial numbness, very bothersome.

(4) Follow-up schedule

All outcome measure data were collected before treatment (baseline) and at the following post-procedure time points: 24 hours, 1 week, 1 month, 3 months, 6 months, 12 months, and 24 months. Data collection was performed during outpatient clinic visits or via structured telephone interviews using standardized case report forms.

Statistical analysis

All statistical analyses were performed using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA). Continuous variables (e.g., age, VAS scores) are presented as mean±standard deviation (SD). Longitudinal changes in VAS scores before and after treatment were analyzed using repeated-measures analysis of variance (ANOVA). Categorical variables (e.g., sex, BNI grades) are expressed as frequencies and percentages (%). All statistical tests were two-tailed, and a P-value <0.05 was considered statistically significant. The Kaplan-Meier survival analysis method was employed to estimate recurrence-free survival rates, and corresponding survival curves were plotted. This method effectively handles censored data within the follow-up period (e.g., patients lost to follow-up or who remained recurrence-free at the study conclusion) and represents the standard analytical approach for evaluating the long-term efficacy of treatments for chronic pain conditions.

Results

Patient baseline characteristics

During the study period, 92 eligible patients were screened. Seven patients declined participation due to personal reasons, resulting in 85 patients being enrolled. All 85 patients underwent the initial ozone neurolysis procedure and completed the full 24-month follow-up. The technical success rate (successful puncture and injection) was 100%.

The demographic and baseline clinical chara-cteristics of the patients are detailed in Table 1. The mean age of the cohort was 76.5±4.2 years (range: 70-88 years old), with 53 females (62.4%). The mean disease duration was 8.1±3.5 years, indicating a protracted chronic course. Pain was predominantly right sided (65.9%, N=56). The most commonly affected trigeminal nerve branches were the combined second and third divisions (V2+V3, 44.7%) and the isolated second division (V2, 30.6%). All patients had experienced treatment failure with at least two prior medication classes before enrollment, with a mean number of failed medication classes of 2.6±0.7. Pre-procedural pain was universally severe, reflected by a mean VAS score of 8.2±0.9 and a BNI pain intensity score of grade V in all patients. No patient reported pre-existing facial numbness (BNI facial numbness grade I).

Table 1. Demographic and baseline clinical characteristics of patients (N=85).

Characteristic		Value	
		N	Ratio (%)
Age (years old)	Mean±SD	76.5±4.2	/
	Range	70-88	/
Sex	Male	32	37.6
	Female	53	62.4

Disease duration (years)	Mean±SD	8.1±3.5	/
Pain laterality	Right	56	65.9
	Left	29	34.1
Affected branches	V1	3	3.5
	V2	26	30.6
	V3	12	14.1
	V1+V2	6	7.1
	V2+V3	38	44.7
Failed medication classes	Mean±SD	2.6±0.7	/
Baseline VAS score (0-10)	Mean±SD	8.2±0.9	/
Baseline BNI pain score	Grade V	85	100.0
Baseline BNI numbness score	Grade I	85	100.0

Note: abbreviations: Visual Analog Scale (VAS); Barrow Neurological Institute (BNI); standard deviation (SD). BNI pain score is an outcome measure for pain intensity and disability.

Pain intensity and neurological dysfunction (VAS and BNI scores)

Following treatment, patients experienced rapid and sustained significant relief in pain intensity. As shown in Table 2 and Figure 2, the mean VAS score decreased significantly from 8.2±0.9 at baseline to 2.5±1.8 at 24 hours post-procedure and remained at low levels throughout the 24-month follow-up period. The reduction in VAS scores at all follow-up time points was highly statistically significant compared to baseline (P<0.001).

The BNI scores similarly demonstrated substantial clinical improvement. At the final 24-month follow-up, 55 patients (64.7%) achieved BNI grade I (completely pain-free, no medication required), 8 patients (9.4%) achieved BNI grade II (occasional mild pain, no medication required), and 6 patients (7.1%) achieved BNI grade III (some pain, satisfactorily controlled with medication).

Overall, a total of 69 patients (81.2%) attained treatment success (defined as BNI grades I-III). Sixteen patients (18.8%) were classified as treatment failures or recurrences (BNI grade IV or V).

Table 2. Pain outcomes at follow-up time points after CT-guided ozone neurolysis.

Timepoint	VAS	P-value	Number & ratio (%)				Treatment success rate (BNI I-III) %
			BNI I	BNI II	BNI III	BNI IV/V	
Baseline	8.2±0.9	/	0 (0.0)	0 (0.0)	0 (0.0)	85 (100.0)	0.0
24 hours	2.5±1.8	<0.001*	48 (56.5)	22 (25.9)	9 (10.6)	6 (7.1)	92.9
1 month	1.8±1.5	<0.001*	60 (70.6)	13 (15.3)	7 (8.2)	5 (5.9)	94.1
6 months	1.9±1.6	<0.001*	58 (68.2)	12 (14.1)	8 (9.4)	7 (8.2)	91.8
12 months	2.0±1.5	<0.001*	56 (65.9)	10 (11.8)	7 (8.2)	12 (14.1)	85.9
24 months	2.1±1.5	<0.001*	55 (64.7)	8 (9.4)	6 (7.1)	16 (18.8)	81.2

Notes: abbreviations: Visual Analog Scale (VAS); Barrow Neurological Institute (BNI); standard deviation (SD). P-values derived from repeated-measures ANOVA comparing VAS scores vs. baseline. Treatment success defined as BNI grades I-III (no pain or adequately controlled pain). Dashes (-) indicate no statistical test performed at baseline.

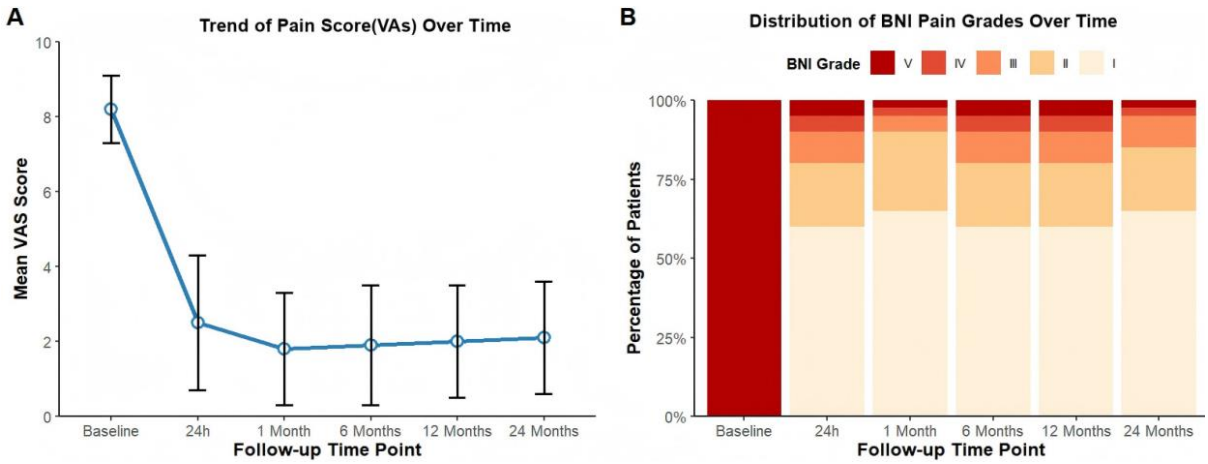

Figure 2. Longitudinal assessment of pain outcomes following CT-guided ozone neurolysis.

Note: (A) Mean Visual Analog Scale (VAS) scores demonstrating sustained pain reduction from baseline to 24 months ($P<0.001$; repeated-measures ANOVA). (B) Barrow Neurological Institute (BNI) Pain Intensity Scores showing progressive improvement, with 81.2% (69/85) achieving treatment success (BNI I-III) at final follow-up. Data presented as mean±SD (VAS) or proportion (BNI). N=85.

Durability of efficacy (Kaplan-Meier Analysis)

During the 24-month follow-up, pain recurrence occurred in 16 patients. Kaplan-Meier survival analysis (Figure 3) estimated recurrence-free survival rates of 91.5% (95% CI: 85.2%-97.8%) at 6 months, 85.3% (95% CI: 77.5%-93.1%) at 12 months, and 78.5% (95% CI: 69.1%-87.9%) at 24 months. These results indicate most patients achieved durable pain relief.

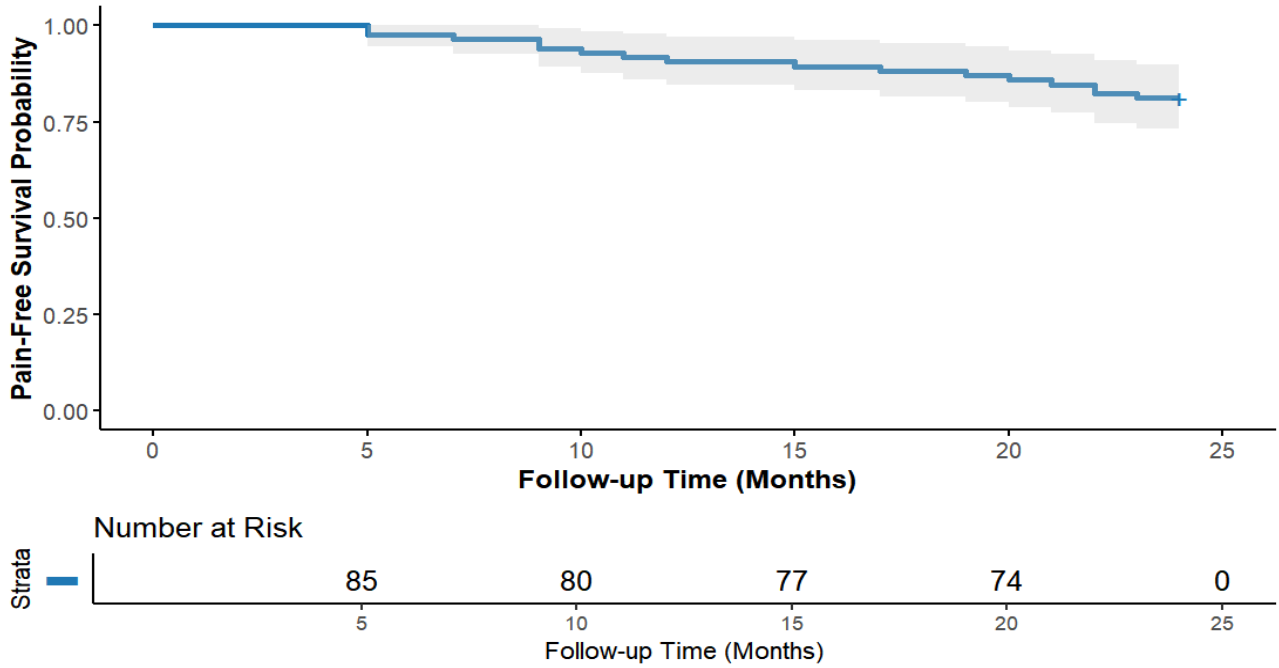

Figure 3. Kaplan-Meier curve for recurrence-free survival.

The curve demonstrates a stepwise decline in survival probability (Y-axis) over time (X-axis, months). A plateau phase is observed in the early period (0-6 months), followed by a modest acceleration in decline, stabilizing at approximately 0.785 by 24 months. The number of patients at risk at each timepoint (0, 6, 12, 18, 24 months) is annotated below the curve.

Safety and tolerability

The procedure was well-tolerated in all elderly patients. No intraoperative complications occurred, including arrhythmia, significant blood pressure fluctuations, intracranial hemorrhage, or nerve injury. All postoperative complications were mild and self-limiting (as shown in Table 3).

The most frequent complication was transient facial hypesthesia, occurring in 10 patients (11.8%). All cases were classified as BNI facial numbness grade II (mild numbness, not clinically bothersome). These symptoms were resolved completely within 24 hours post-procedure, with no residual permanent sensory deficits observed. The second most common complication was minor local hematoma at the puncture site (4 cases, 4.7%), all of which resolved rapidly with conservative local compression. Transient mild masticatory weakness was observed in 2 patients (2.4%), and herpes labialis recurrence occurred in 3 patients (3.5%). Critically, no instances of severe or bothersome facial numbness (BNI grade III/IV), anesthesia dolorosa, keratitis, meningitis, or other permanent neurological deficits occurred in this patient cohort.

Table 3. Incidence of postoperative complications (N=85).

Complication	Cases (N)	Incidence (%)	Remarks
Transient facial hypesthesia (BNI grade II)	10	11.8	Resolved completely within 24 hours in all cases
Puncture site hematoma	4	4.7	Minor; resolved spontaneously
Transient mild masticatory weakness	2	2.4	Resolved within 1 month in all cases

Complication	Cases (N)	Incidence (%)	Remarks
Herpes labialis recurrence	3	3.5	Resolved with standard antiviral therapy
Severe facial numbness (BNI grade III/IV)	0	0.0	/
Anesthesia dolorosa	0	0.0	/
Keratitis	0	0.0	/
Intracranial infection/hemorrhage	0	0.0	/

Note: Postoperative Complication Profile Within 24-Month Follow-up Period (N=85 Elderly Trigeminal Neuralgia Patients Undergoing CT-Guided Ozone Neurolysis).

Repeat treatment

Among the 16 patients with recurrent pain, 12 elected to undergo a second ozone neurolysis procedure. All 12 patients (100%) re-achieved satisfactory pain relief (BNI grades I-III) following retreatment, with no new or more severe complications observed.

Discussion

This prospective cohort study provides the first systematic evaluation of the long-term efficacy and safety of CT-guided ozone neurolysis of the Gasserian Ganglion in elderly patients (≥70 years old) with Idiopathic Trigeminal Neuralgia (ITN). Our findings demonstrate that this technique offers substantial, effective, and durable pain relief with an exceptional safety profile for this vulnerable population. Over the two-year follow-up, >80.0% of patients maintained satisfactory pain control without serious or permanent complications, delivering robust evidence for managing refractory ITN in the elderly.

The efficacy outcomes reported here compare favorably with other minimally invasive techniques. The 24-month recurrence-free survival rate (78.5%) aligns with reported outcomes for radiofrequency thermocoagulation (RFT) and percutaneous balloon compression (PBC) [21]. Although potentially modestly lower than microvascular decompression (MVD) success rates in optimal candidates, this comparable efficacy was achieved in a high-risk cohort (mean age >76 years old with prevalent comorbidities). Critically, ozone neurolysis achieves therapeutic effects through a fundamentally distinct mechanism compared to neuroablative procedures - constituting its core clinical advantage.

The most salient finding is the procedure's exemplary safety profile, directly attributable to its non-neurodestructive mechanism. Conventional percutaneous neuroablation (RFT, PBC) relies on irreversible damage to trigeminal sensory fibers. Consequently, facial numbness - reported in 100% of PBC patients with pain relief - is not merely a common complication but often an indicator of treatment efficacy [22]. These sensory deficits may become permanent, significantly bothersome, or progress to anesthesia dolorosa [23]. In stark contrast, only 11.8% of our cohort developed transient facial hypesthesia (all BNI grade II), resolving completely within 24 hours. This profound neural preservation addresses the inherent trade-off of neuroablative techniques: pain relief at the cost of function. Furthermore, as a percutaneous minimally invasive technique, ozone neurolysis circumvents the major systemic risks associated with MVD (e.g., stroke, intracranial infection, hematoma, mortality) - risks substantially amplified in the elderly [24]. Thus, its safety profile ideally fills a therapeutic gap for elderly patients unsuitable for MVD's systemic risks or unwilling to accept neuroablative functional sequelae.

Another key finding is the technique's repeatability. ITN is a chronic relapsing disorder, and recurrence necessitates retreatments [25,26]. Repeat MVD carries increased technical difficulty and risk, while repeated neuroablation compounds cumulative nerve damage - heightening risks of severe sensory loss and anesthesia dolorosa. In our study, all 12 retreated patients re-achieved BNI I-III pain relief without incremental complications. This underscores how ozone neurolysis' non-destructive nature enables sustainable long-term management. For elderly patients, shifting therapeutic goals from pursuing "curative ablation" toward "safe, effective long-term control" through a low-risk, repeatable approach represents a pragmatic and patient-centered strategy - prioritizing years of high-quality pain-free life over

uncertain durability achieved through higher-risk interventions.

Several limitations warrant careful consideration. The primary limitation is the single-arm, uncontrolled design. Without placebo or active comparators, we cannot fully distinguish true treatment effects from natural disease history or potent placebo effects - particularly relevant in pain intervention studies where expectations of high-tech procedures (e.g., CT-guided injection) may activate endogenous analgesia. While the magnitude and durability of pain relief align with ozone's known biological mechanisms and make pure placebo attribution unlikely, we cannot quantify its contribution. Secondly, the single-center design and modest sample size may limit generalizability.

Despite these limitations, our promising findings establish a foundation for higher-level evidence. Future research should prioritize multicenter randomized controlled trials (RCTs): Either placebo-controlled to isolate treatment effects, or head-to-head comparisons against established therapies (e.g., RFT) to directly evaluate efficacy and safety - particularly long-term nerve preservation. Such studies will definitively position ozone neurolysis within the elderly ITN treatment algorithm.

Conclusion

In this prospective cohort study of elderly patients (≥70 years old) with refractory ITN, CT-guided ozone neurolysis of the Gasserian Ganglion is proved to be a highly effective, safe, and durable therapeutic approach, providing stable pain control over a 24-month follow-up. Its non-neurodestructive mechanism, exceptional safety profile, and repeatability make it an ideal option for this fragile population, effectively mitigating the significant risks of traditional craniotomy and neuroablative procedures. Future randomized controlled trials are warranted to corroborate these promising findings.

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Authors' contributions

Concept and design: Maojiang Yang, Xian Qiong, Hanfeng Yang. Acquisition of data: Xian Qiong, Hongying Yang. Analysis and interpretation of data: Qiong Xian, Maojiang Yang. Drafting of the manuscript: Maojiang Yang, Xiaoxue Xu. Revising it for intellectual content: Hanfeng Yang, Husni Ahmed Abdullah Al-Goshae. Final approval of the completed manuscript: all authors. Maojiang Yang, Xian Qiong and Hongying Yang contribute equally to the article.

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Conflicts of Interest

The authors declare no conflict of interest.

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