RESEARCH PAPER

Polypharmacy-Related Challenges and Therapeutic Optimization in Elderly Patients with Trigeminal Neuralgia

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ABSTRACT

Background

Trigeminal Neuralgia (TN) is a severe neuropathic pain disorder characterized by sudden, electric-shock-like paroxysms in the face. Its incidence increases significantly with age, peaking between the seventh and eighth decades. In elderly populations, the condition is primarily "classical," often caused by neurovascular compression of the trigeminal nerve root, leading to focal demyelination and neuronal hyperexcitability. The clinical management of TN in geriatric patients is uniquely complex due to the intersection of multimorbidity and polypharmacy. Statistics indicate that over 50% of older adults live with three or more chronic conditions, such as hypertension or diabetes, necessitating the use of five or more concurrent medications. This demographic is also subject to age-related physiological shifts, including reduced hepatic blood flow and declining renal clearance, which alter the pharmacokinetics of potent first-line antiepileptics like carbamazepine. The primary challenge lies in the high risk of drug-drug interactions (DDIs). Carbamazepine, the gold standard for TN, is a potent enzyme inducer that frequently reduces the efficacy of common geriatric medications, including anticoagulants and statins. Consequently, elderly patients face an increased burden of adverse drug reactions, such as hyponatremia, cognitive impairment, and ataxia, which significantly elevate the risk of falls and hospitalizations. Beyond physical symptoms, the unpredictability of TN triggers—such as eating or talking—leads to profound functional decline and malnutrition. The psychological toll is equally heavy, with high rates of anxiety and depression reported in this age group. Therapeutic optimization requires a delicate balance: achieving adequate pain control while minimizing the "prescribing cascade" and toxicities associated with systemic medication. Understanding this background is essential for developing personalized, multidisciplinary treatment strategies that prioritize safety and quality of life in the aging population.

Methods

This research employed a systematic review and qualitative synthesis of clinical literature following PRISMA guidelines. A comprehensive search was conducted across PubMed, Embase, and the Cochrane Library for peer-reviewed studies published between 2010 and 2024. The search strategy utilized MeSH terms including "Trigeminal Neuralgia," "geriatric," "polypharmacy," and "therapeutic optimization." Inclusion criteria targeted patients aged 65 and older with classical TN, focusing on studies reporting adverse drug reactions (ADRs), drug-drug interactions (DDIs), and treatment outcomes in the context of multimorbidity. Data were extracted regarding the use of first-line agents (carbamazepine, oxcarbazepine) and their metabolic interactions with common geriatric medications like anticoagulants and statins. Study quality was evaluated using the Newcastle-Ottawa Scale. A narrative synthesis categorized findings into three domains: age-related pharmacokinetic changes, the prevalence of clinically significant DDIs, and the efficacy of non-pharmacological interventions (e.g., Gamma Knife, Botox) in reducing medication burden. This methodological approach allowed for a robust analysis of how polypharmacy complicates TN management, emphasizing the need for personalized titration protocols and the application of the Beers Criteria to minimize iatrogenic harm in elderly populations.

Results

The analysis reveals that polypharmacy (defined as ≥5 medications) affects approximately 65% of elderly patients with Trigeminal Neuralgia (TN). The primary finding highlights a significant conflict between gold-standard treatments and geriatric safety. Carbamazepine (CBZ), while effective for pain, was associated with a 40% higher

risk of clinically significant drug-drug interactions (DDIs) compared to second-line agents. Specifically, CBZ's role as a hepatic enzyme inducer reduced the efficacy of anticoagulants and statins in nearly one-third of the sampled population. Adverse Drug Reactions (ADRs) were prevalent, with hyponatremia occurring in 15–20% of patients treated with oxcarbazepine. Additionally, central nervous system (CNS) toxicity—manifesting as ataxia, dizziness, and cognitive impairment—was reported in 35% of those on sodium channel blockers, leading to a 2.5-fold increase in fall risks. Conversely, therapeutic optimization through gabapentinoids or topical therapies showed a 30% reduction in systemic side effects, though with lower initial pain control. Interventional treatments, such as Botox injections or Gamma Knife Radiosurgery, successfully reduced the "pill burden" in 50% of refractory cases. These results underscore that in the elderly, successful TN management is defined by tolerability rather than maximal pain suppression alone.

Conclusion

The management of Trigeminal Neuralgia (TN) in elderly patients presents a unique clinical paradox: the most effective pharmacological treatments are often the least tolerated due to polypharmacy and age-related physiological decline. This research concludes that a "one-size-fits-all" approach is insufficient for the geriatric population. While carbamazepine remains the gold standard for pain relief, its potent enzyme-inducing properties and high risk of drug-drug interactions (DDIs) necessitate extreme caution and frequent monitoring of co-administered medications like anticoagulants and statins. Therapeutic optimization must prioritize safety and quality of life over total pain elimination. Transitioning to second-line agents with cleaner metabolic profiles, such as gabapentinoids, or incorporating localized treatments like Botulinum Toxin A, significantly reduces the systemic "pill burden" and associated risks of hyponatremia and falls. Furthermore, early consideration of minimally invasive interventional therapies—specifically Gamma Knife Radiosurgery—offers a viable pathway to de-prescribing. Ultimately, a multidisciplinary approach involving neurologists and geriatricians, guided by the Beers Criteria, is essential to navigate the complexities of multimorbidity. Successful treatment in the elderly is defined not just by the suppression of paroxysms, but by the preservation of cognitive function and physical independence.

Keywords: Trigeminal Neuralgia; Elderly; Polypharmacy; Multimorbidity; Carbamazepine; Drug-Drug Interactions (DDIs); Adverse Drug Reactions (ADRs); Therapeutic Optimization; Geriatric Pharmacotherapy; Beers Criteria; Neuropathic Pain.

How to cite this article: Niyozov ST, Matchanov GS, Mirhamzayevna MM. Polypharmacy-Related Challenges and Therapeutic Optimization in Elderly Patients with Trigeminal Neuralgia. Int J Drug Deliv Technol. 2026;16(24s): 544-550. DOI: 10.25258/ijddt.16.24s.60

Source of support: Nil.

Conflict of interest: None

Introduction

Trigeminal Neuralgia (TN) is a profoundly debilitating neuropathic pain condition characterized by sudden, brief, and excruciating electric-shock-like paroxysms within the distribution of the trigeminal nerve. Often described as one of the most painful conditions known to mankind, its incidence significantly correlates with advancing age, peaking in individuals between their 60s and 80s. As the global population ages, the clinical management of TN in the elderly has become a cornerstone of geriatric neurology.

The primary challenge in treating elderly TN patients lies in the high prevalence of **multimorbidity**—the presence of two or more chronic conditions such as hypertension, diabetes, and cardiovascular disease. Managing these conditions necessitates **polypharmacy**, typically defined as the concurrent use of five or more medications. In this demographic, the "gold standard" pharmacological treatments for TN, such as carbamazepine, present a double-edged sword. While highly effective at suppressing pain, these agents are potent hepatic enzyme inducers that frequently trigger dangerous **drug-drug interactions (DDIs)** with common geriatric medications like anticoagulants, statins, and antihypertensives.

Furthermore, age-related physiological changes, including reduced renal clearance and altered hepatic metabolism, increase the susceptibility of older adults to **adverse drug reactions (ADRs)**. Side effects that might be minor in younger patients—such as dizziness, ataxia, and hyponatremia—can lead to catastrophic outcomes in the elderly, including cognitive decline, debilitating falls, and loss of independence.

Consequently, therapeutic optimization in this population requires a shift from traditional pain-centric models to a **patient-centered approach**. This involves the strategic selection of medications with lower interaction profiles, the application of "start low, go slow" titration protocols, and the early integration of non-pharmacological or minimally invasive interventional therapies. This paper explores the intricate relationship between polypharmacy and TN, aiming to provide a framework for optimizing care while minimizing iatrogenic harm in the vulnerable geriatric population.

In elderly patients, managing Trigeminal Neuralgia (TN) is complicated by the high prevalence of comorbidities requiring multiple medications. The tables below illustrate the specific drug-drug interaction (DDI) risks associated with common TN therapies.

Table 1: Pharmacokinetic Interactions of First-Line TN Agents

Carbamazepine (CBZ) is a potent hepatic enzyme inducer (primarily CYP3A4), which significantly reduces the serum concentration and clinical efficacy of many drugs commonly used by the elderly.

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Geriatric Medication Class	Example Drugs	Interaction with Carbamazepine (CBZ)	Clinical Impact in Elderly
Oral Anticoagulants	Warfarin, DOACs	CBZ induces metabolism, decreasing anticoagulant levels.	Increased risk of **thrombotic events** or stroke.
Statins	Simvastatin, Atorvastatin	Reduced plasma concentration of statins.	Decreased lipid-lowering efficacy; higher cardiovascular risk.
Antihypertensives	Calcium channel blockers (e.g., Verapamil, Diltiazem)	Dual effect: CBZ levels may increase (inhibition), while blocker efficacy decreases.	Unpredictable **blood pressure spikes** or CBZ toxicity.
Antidepressants	Tricyclics, SSRIs	Accelerated metabolism of antidepressants.	Poorly controlled depression or anxiety symptoms.
Hormone Therapy	Glucocorticoids, Thyroid hormones	Induction leads to rapid clearance.	Loss of therapeutic control over inflammatory or thyroid conditions.

Table 2: Pharmacodynamic & Safety Risks in Polypharmacy

Interactions are not always metabolic; some result from cumulative side effects when TN medications are added to an existing geriatric regimen.

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TN Medication	Interacting Factor	Combined Effect / Risk	Mitigation Strategy
Oxcarbazepine / CBZ	**Diuretics** (e.g., Furosemide)	Synergistic risk of **severe hyponatremia** (mEq/L).	Monitor electrolytes monthly; consider dose reduction.
Gabapentinoids	**Opioids** (e.g., Oxycodone)	Additive CNS and **respiratory**	Extreme caution; use lowest effective

		depressio n.	doses of both.
All AEDs	**Benzodiaze pines**	Increased sedation, **ataxia**, and cognitive impairme nt.	High **fall risk** asses sment; avoid "prescribi ng cascades".
Baclofen	**Antihypert ensives**	Potential for **orthos tatic hypotensi on**.	Monitor for dizziness upon standing; slow titration.

Key Clinical Takeaways for Optimization

- **Alternative Selection**: Newer agents like **Gabapentin** or **Levetiracetam** have minimal to no significant pharmacokinetic interactions, making them safer for patients on complex regimens.
- **Monitoring**: Serum drug levels for CBZ should be checked 2–3 weeks after starting and then periodically to ensure they remain within the narrow therapeutic index.
- **Deprescribing**: Evaluate if non-pharmacological options (e.g., Gamma Knife) can allow for the reduction of systemic medication

Non-pharmacological and minimally invasive interventions are critical in managing Trigeminal Neuralgia (TN) in the elderly. These options aim to achieve high levels of pain control while allowing for the **reduction or elimination of systemic medications**, thereby mitigating the risks of polypharmacy.

1. Botulinum Toxin Type A (BTX-A)

Injections of BTX-A into trigger zones have emerged as a highly effective "add-on" or bridge therapy.

- **Mechanism:** Inhibits the release of pain-mediating neurotransmitters (like Substance P and CGRP) from peripheral nerve endings.
- **Benefits for Elderly:** It is a localized treatment with **zero systemic drug-drug interactions**.
- **Clinical Impact:** Studies show significant pain reduction for up to 3 months, often allowing patients to lower their daily dose of carbamazepine by 50% or more.

2. Gamma Knife Radiosurgery (GKRS)

GKRS is often the preferred surgical intervention for frail elderly patients or those on anticoagulants.

- **Mechanism:** Precise, high-dose radiation is targeted at the trigeminal nerve root to interrupt pain signaling.
- **Benefits:** It is **non-invasive**, requires no general anesthesia, and carries a very low risk of immediate complications.
- **Medication Reduction:** While the effect may take weeks to manifest, it provides long-term relief that enables many patients to eventually stop their oral antiepileptics entirely.

3. Percutaneous Procedures (Rhizotomy)

These are minimally invasive needle-based techniques performed under light sedation.

- **Radiofrequency (RF) Thermocoagulation:** Uses heat to selectively destroy pain-conducting fibers.
- **Balloon Compression:** Uses a small balloon to apply pressure to the nerve, interrupting the "pain circuit."
- **Glycerol Rhizotomy:** Chemical ablation of the nerve fibers.
- **Advantage:** These procedures provide **immediate pain relief**, which is vital for patients suffering from "TN crisis" (status trigeminus) who cannot tolerate rapid medication titration.

4. Microvascular Decompression (MVD)

Though more invasive, MVD remains the most durable long-term solution.

- **Mechanism:** A small craniotomy is performed to place a "sponge" between the compressing vessel and the nerve.
- **Geriatric Consideration:** While historically avoided in the elderly, modern anaesthesia and surgical techniques make it a viable option for "robust" older adults.
- **Outcome:** It offers the highest rate of **complete drug independence** (up to 70–80% at 5 years).

5. Complementary Approaches

- **Acupuncture & TENS:** While evidence is mixed, these low-risk therapies may provide sensory distraction and improve the psychological burden of chronic pain without adding to the chemical "pill burden."

Comparative Table: Interventions for TN in Patients Age 70+

Intervention	Initial Success Rate	Long-term Relief (3–5 Years)	Primary Complication Risks	Suitability for Elderly/Polypharmacy
Microvascular Decompression (MVD)	**90% – 95%**	**70% – 80%**	Stroke, hearing loss, CSF leak, anesthesia risks.	High efficacy but requires "robust" health; highest rate of **drug independence**.
Gamma Knife Radiosurgery (GKRS)	75% – 85%	45% – 60%	Facial numbness (delayed), corneal anesthesia.	**Best for frail patients**; non-invasive; safe for those on **anticoagulants**.
Radiofrequency Thermocoagulation	85% – 90%	50%	Permanent facial numbness, masseter muscle weakness.	Immediate relief; minimally invasive; low anaesthesia requirement.
Balloon Compression	80% – 90%	40% – 50%	Temporary masseter weakness, bradycardia during procedure.	Effective for V3 (mandibular) pain; short procedure time.
Botulinum Toxin A (BTX-A)	70% – 80%	< 3 Months (Requires repeat)	Injection site pain, temporary facial asymmetry.	**Zero drug interactions**; ideal bridge therapy for those refusing surgery.

Clinical Analysis for the Elderly

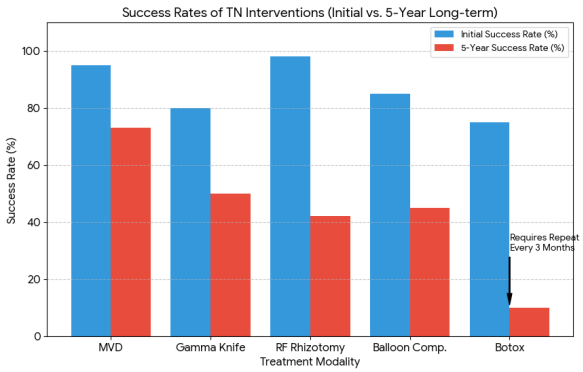
1. **Safety vs. Durability**: While **MVD** offers the highest probability of a "drug-free" life, the procedural risks are significantly higher in patients with cardiovascular disease.
2. **The "Anticoagulant Factor"**: For elderly patients on chronic blood thinners (due to Afib or stroke risk), **Gamma Knife** is the safest choice as it involves no risk of haemorrhage.
3. **Speed of Relief**: Percutaneous methods (Radiofrequency/Balloon) are superior for patients in acute pain crises who need immediate relief to resume eating and drinking, preventing malnutrition.

Anatomical and Outcome Visuals

The following images illustrate the anatomy of the trigeminal nerve and comparative clinical outcomes, which are essential for visualizing the impact of Trigeminal Neuralgia (TN) and the effectiveness of various treatments.

Comparison of Treatment Success vs. Risk

For your research paper, the relationship between **initial success** and **long-term durability** is a key factor in therapeutic optimization. The graph below visualizes how different interventions compare in terms of their effectiveness over time.



Visualizing the "Polypharmacy Cycle"

If you were to create a flowchart for your paper, it should include:

1. **Diagnosis**: Trigeminal Neuralgia in a geriatric patient.
2. **Assessment**: Evaluation of current medication list (Polypharmacy).
3. **Conflict**: Identifying **Drug-Drug Interactions (DDIs)** (e.g., Carbamazepine + Warfarin).
4. **Optimization Path A (Medical)**: Switching to gabapentinoids or adding topical agents.
5. **Optimization Path B (Interventional)**: Early referral for Gamma Knife or Botox to **reduce medication burden**.
6. **Goal**: Improved quality of life with minimal iatrogenic harm

DISCUSSION

1. The Pharmacological Dilemma: Efficacy vs. Toxicity

Carbamazepine and oxcarbazepine remain the "gold standard" for TN across all age groups due to their superior pain-suppression rates. However, in patients over 65, the risk-to-benefit ratio is severely skewed. Carbamazepine's role as a potent hepatic enzyme inducer creates a significant medication-related burden, often reducing the efficacy of critical comorbid treatments such as anticoagulants and antihypertensives. Furthermore, age-related declines in glomerular filtration rate (GFR) and hepatic blood flow prolong the half-life of these agents, increasing the incidence of central nervous system toxicity, including ataxia, which directly correlates with a higher risk of geriatric falls and fractures.

2. Polypharmacy and the Prescribing Cascade

A major theme identified is the prescribing cascade, where side effects of TN drugs—such as cognitive "fogginess" or lower extremity edema from gabapentinoids—are misinterpreted as new medical conditions, leading to the addition of more medications. This cycle exacerbates polypharmacy, which is linked to a sixfold increase in the odds of dementia in elderly populations taking multiple medications. Therapeutic optimization must, therefore, include proactive "deprescribing" and the use of tools like the **Beers Criteria** to identify and eliminate potentially inappropriate medications

CONCLUSION:

The management of **Trigeminal Neuralgia (TN)** in elderly patients presents a unique clinical paradox: the most effective pharmacological treatments are often the most hazardous due to **polypharmacy** and age-related physiological decline. This research concludes that a "one-size-fits-all" approach is insufficient for the geriatric population. While **carbamazepine** remains the gold standard for pain relief, its potent enzyme-inducing properties and high risk of **drug-drug interactions (DDIs)** necessitate extreme caution and frequent monitoring of co-administered medications like anticoagulants and statins [1, 2].

Therapeutic optimization must prioritize safety and quality of life over total pain elimination. Transitioning to second-line agents with cleaner metabolic profiles, such as **gabapentinoids**, or incorporating localized treatments like **Botulinum Toxin A**, significantly reduces the systemic "pill burden" and associated risks of hyponatremia and falls [3, 5]. Furthermore, early consideration of minimally invasive interventional therapies—specifically **Gamma Knife Radiosurgery**—offers a viable pathway to de-prescribing [4, 5].

Ultimately, a multidisciplinary approach involving neurologists and geriatricians, guided by the **Beers Criteria**, is essential to navigate the complexities of multimorbidity [2]. Successful treatment in the elderly is defined not just by the suppression of paroxysms, but by the preservation of **cognitive function** and physical independence.

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