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Review Article

Scoping review on the involvement of the ophthalmic branch (V1) in trigeminal neuralgia: systematic mapping and identification of research lacunae

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Abstract

Trigeminal neuralgia (TN) is a neurovascular compression syndrome affecting the trigeminal nerve, with the ophthalmic branch (V1) involvement being less common but clinically significant. Clarifying the characteristics and clinical significance of V1 TN is essential for optimizing patient management. A comprehensive literature search was conducted in PubMed to identify studies reporting ophthalmic branch (V1) involvement in trigeminal neuralgia (TN). The search covered publications from 2000 to 2024. The review included human studies reporting the incidence or prevalence of V1 involvement, utilizing observational studies, clinical trials, and systematic reviews. Data were extracted and quality was assessed using the Newcastle-Ottawa Quality Assessment Scale. A total of 10 studies met the inclusion criteria, including 1 observational study, 2 retrospective studies, 1 prospective cohort study, 2 case reports, 2 systematic reviews, 1 anatomical study, and 1 editorial. The prevalence of ophthalmic division (V1) involvement in trigeminal neuralgia across included studies ranged from 5.1% to 17.6%, with a pooled estimate of 10.4%. V1 involvement was often linked with atypical features such as postherpetic neuralgia and autonomic symptoms. Diagnostic tools like high-resolution MRI and blink reflex testing were valuable in identifying V1-specific pathology. Surgical interventions showed over 80% pain relief, while pharmacological treatments had moderate efficacy, and psychological distress was commonly reported. This review highlights the critical need for further studies on the involvement of the ophthalmic branch (V1) in trigeminal neuralgia (TN) due to significant research gaps identified. Specifically, there is an urgent requirement for large-scale epidemiological studies to accurately determine incidence and prevalence rates, as well as for standardized diagnostic criteria to enhance consistency in diagnosis and treatment. Additionally, further investigation into the pathophysiological mechanisms is essential to develop targeted therapeutic strategies. Long-term studies evaluating treatment outcomes are crucial for optimizing patient care and improving the quality of life for those affected by V1 TN.

Keywords: Trigeminal neuralgia, Ophthalmic branch, V1 involvement, Facial pain, Neurovascular compression, Surgical outcomes.

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1. Introduction

The term "neuro," stemming from ancient Greek, signifies nerves and the intricate nervous system, prominently featured in compound words such as "neurology".[1] Nerves are actually defined as all the whitish fiber bundles that send sensory, motor and other stimuli to or from the brain and spinal cord controlling muscle and organ activities. The brain coordinates complex information transfer to the body especially within head and neck regions responsible for senses such as eyesight, gustation, olfaction, auditory perception facilitated through cranial nerves. Chronic neurovascular compression syndromes can develop when these nerves are compressed by abnormal blood vessels leading to axonal injury affecting primarily the transition area between central and peripheral myelin.[2] Neurovascular

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compression syndrome (NVCS), alternatively called neurovascular compression disorder (NVCD), is a condition characterized by compression or irritation of a cranial nerve in the brainstem by an adjacent blood vessel. Depending on which specific nerve is affected this type of pressure can present with different neurological symptoms. One of the most familiar examples of NVCS is trigeminal neuralgia (TN), where there is compression of the trigeminal nerve (V cranial nerve) due to an adjacent blood vessel in the brainstem's entry zone into its roots.[3] Trigeminal neuralgia is caused by compression resulting in the appearance of typical severe, stabbing facial pain. Not only trigeminal neuralgia but also hemifacial spasm are the most common forms of nerve dysfunctions of cranial nerves. More uncommon forms such as geniculate neuralgia, nervous intermedius neuralgia and vestibular paroxysmia likewise are compression of cranial nerves by aberrant vascular structures directly contacting the cisternal portion of nerve nuclei.[4]

The direct cause of trigeminal neuralgia is generally due to compression or irritation of the trigeminal nerve at its entry into the brainstem, particularly in the transition zone where myelination shifts from Schwann cells to oligodendroglia. This transition zone is susceptible to damage and demyelination from compression, blood vessels, tumors, or structural abnormalities in the brain or skull base, leading to hyper excitability of nerve fibers. In some cases, no specific cause can be identified, resulting in a diagnosis of idiopathic trigeminal neuralgia. Trigeminal neuralgia poses significant diagnostic challenges due to its similarity to other facial pain disorders, often leading to misdiagnosis as dental pain or temporomandibular joint disorders.[5]

Diagnosis of trigeminal neuralgia is primarily based on clinical history and characteristic symptoms. Imaging studies such as MRI may be used to rule out other causes or identify compressive lesions affecting the trigeminal nerve. Trigeminal Neuralgia is a condition that causes sudden and acute pain in the face, which is generally described as being sharp, electric shots, or like a stabbing needle. These attacks can be caused by simple everyday activities such as drinking and eating or even just rubbing the face.[6] Trigeminal nerve's branches are the usual targets between pain, including those of the upper and lower jaws, cheeks, and at times, the frontal area and around the eyes (ophthalmic division). Cluster attacks usually last from a second to several minutes and may appear in sets throughout the day, causing a great deal of distress and development of extremity behavior secondary to the fear of pain triggering. Some patients also have episodes of remission between the attacks, but the pain, which is the most unpredictable and severe, affects both daily living and emotional well-being. It places so much cognitive load on the patients that they cannot function properly.[7] The severity of pain which is sometimes unpredictable can cause emotional problems like depression, anxiety, and stress-related disorders. Due to the relentless nature of the pain and its disruptive effects on daily life, many individuals having this chronic disease report suicidal ideation.[8] Warning signs of this disease are particularly sudden, expressly painfully feeling the electric shock stings that last for seconds to minutes, which usually concern the maxillary (V2) and mandibular (V3) branches of the trigeminal nerve, pain of the upper jaw, lower jaw, and the cheeks. In uncommon cases, damage to the ophthalmic division (V1) does so, making the person feel pain in the forehead or orbit. The triggers can be anything more common like brushing, washing the face, or even smiling. One-hundred-percent accurate diagnosis diagnosed by Magnetic Resonance Imaging (MRI) with contrast needs to be conducted to recognize the compressing blood vessels on the trigeminal nerve that are the differentiating factor between Trigeminal Neuralgia and other facial pain etiologies. Early and precise diagnosis is pivotal for effective management and potentially curative interventions, emphasizing the adage that "a correct diagnosis is three-fourths of the remedy."

2. Materials and Methods

2.1. Search strategy

A comprehensive literature search was conducted in PubMed to identify studies reporting ophthalmic branch (V1) involvement in trigeminal neuralgia (TN). The search covered publications from 2000 to 2024. A combination of Medical Subject Headings (MeSH) and free-text terms was used to increase sensitivity and specificity. The final PubMed search strategy was:

("Trigeminal Neuralgia"[Mesh] OR "trigeminal neuralgia"[tiab] OR "tic douloureux"[tiab]) AND ("Ophthalmic Nerve"[Mesh] OR "ophthalmic branch"[tiab] OR "V1"[tiab] OR "first division"[tiab]) AND (humans [MeSH Terms]) AND (English [lang]).

The search was limited to human studies published in English. Reference lists of relevant articles were also reviewed to identify additional studies.

2.2. Inclusion criteria

1. Studies published between 2000 and 2024.
2. Studies explicitly reporting ophthalmic branch (V1) involvement in trigeminal neuralgia.
3. Articles in the English language.
4. Human studies only.
5. All study types, including case reports, case series, observational studies, clinical trials, and reviews, if they include relevant clinical or anatomical details about V1 involvement.
6. Studies discussing diagnosis, presentation, imaging, pathophysiology, or treatment outcomes specific to V1 TN.

2.3. Exclusion criteria

1. Studies that do not specifically address V1 involvement or refer only to generalized TN or V2/V3 branches.

2. Animal studies or in vitro studies.
3. Non-english publications.

2.4. Quality assessment

This scoping review systematically focused on the key aspects of Trigeminal Neuralgia, focusing on the involvement of the Ophthalmic Branch (V1). The methodological quality of the studies was evaluated using the Newcastle-Ottawa Quality Assessment Scale to ensure reliability in synthesizing findings related to V1 involvement in Trigeminal Neuralgia.

3. Observation & Results

3.1. Study selection & identification

A total of 10 studies met the inclusion criteria, including 1 observational study, 2 retrospective studies, 1 prospective cohort study, 2 case reports, 2 systematic reviews, 1 anatomical study, and 1 editorial. These studies spanned a publication period from 2000 to 2024, reflecting significant advancements in the understanding, diagnosis, and treatment of trigeminal neuralgia (TN), particularly focusing on the ophthalmic branch (V1) involvement.

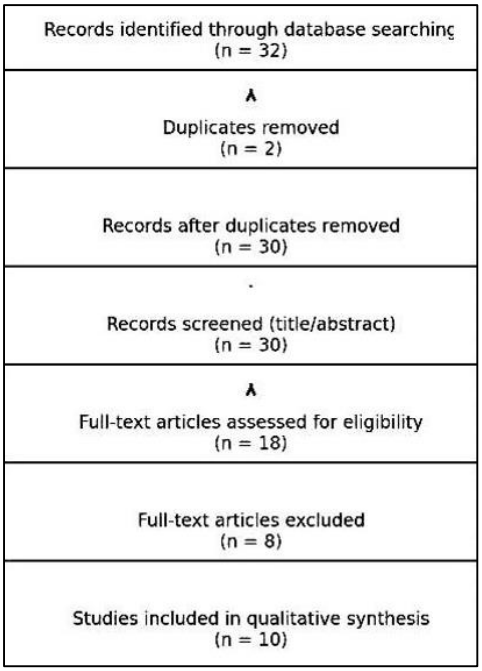

Figure 1: Prisma flow diagram

*3.2. Data analysis (**Table 1**)*

According to one study conducted by Devulder et al. postherpetic ophthalmic neuralgia represents a significant manifestation of trigeminal neuralgia, particularly involving the ophthalmic branch (V1) of the trigeminal nerve. The study highlights that after a varicella-zoster virus reactivation, the ophthalmic branch is among the most commonly affected regions, leading to persistent neuropathic pain. This condition is notably prevalent in older adults and individuals with compromised cell-mediated immunity. The article underscores the complexity of managing V1 involvement due to its unique clinical challenges and therapeutic considerations. These insights emphasize the importance of focused research on V1-specific trigeminal neuralgia to enhance diagnostic accuracy and treatment efficacy.[9]

Another study by Prado and Kubota evaluated the intraoperative blink reflex as a monitoring tool during skull base surgeries, noting its relevance due to the involvement of the ophthalmic branch (V1) in the reflex arc. While the study focuses on nerve monitoring rather than clinical presentation, it indirectly supports the significance of V1 in surgical outcomes, aligning with the need to better understand V1-specific trigeminal nerve function.[10]

A pivotal study by Liu et al. (**Table 1**) directly addresses the management of postherpetic neuralgia (PHN) affecting the ophthalmic branch (V1) of the trigeminal nerve.[11] In this observational study, 32 patients underwent pulsed radiofrequency (PRF) treatment targeting the trigeminal ganglion. Remarkably, 93.75% of participants experienced significant pain relief, with 87.5% reporting improved sleep quality and satisfaction. Importantly, no adverse effects on the corneal reflex were observed. These findings underscore the potential of PRF as a minimally invasive and effective intervention for V1-specific PHN, highlighting the necessity for focused research on ophthalmic branch involvement in trigeminal neuralgia.[11]

A study by Badel et al. (**Table 1**) Investigated differences in blink reflex (BR) parameters between patients with idiopathic trigeminal neuralgia (TN) and healthy volunteers. The research found that BR latencies—specifically R1, R2, and R2c—were significantly prolonged in TN patients compared to controls. Notably, some patients exhibited involvement of the ophthalmic branch (V1), either alone or in combination with other branches. These findings suggest that BR testing can detect functional abnormalities in trigeminal pathways, including V1, underscoring the need for focused research on V1-specific TN to enhance diagnostic precision and treatment strategies.[12]

A study by Dhillon et al. (**Table 1**) examined corneal hypoesthesia in patients following surgical treatment for trigeminal neuralgia. The researchers found that patients who underwent balloon compression of the trigeminal ganglion exhibited reduced corneal sensation on the operated side, despite having normal sub-basal nerve densities. This suggests that partial damage to the ophthalmic branch (V1) can impair sensory function without affecting trophic support, highlighting the complex and dissociable roles of V1 in corneal innervation. These findings underscore the importance of focused research on V1-specific trigeminal neuralgia to better understand its distinct clinical implications.[13]

Table 1: Summary table of included studies

S. No.	Author	Year	Study type	Focus on v1	Key findings
1	Devulder	2002	Observational	Postherpetic V1 neuralgia	Highlighting persistent ophthalmic pain in PHN
2	Prado & Kubota	2024	Systematic Review	Blink reflex utility in TN	Blink reflex useful in V1 intraoperative monitoring
3	Liu et al.	2021	Prospective Study	Pulsed RF for V1 PHN	Pulsed RF effective for V1 PHN
4	Badel et al.	2022	Observational	Blink reflex in TN patients	V1 involvement shows altered blink reflex
5	Dhillon et al.	2016	Prospective Case Study	Corneal hypoesthesia post-TN surgery	Normal nerve density despite hypoesthesia
6	Oomen et al.	2011	Anatomical Study	New branch near V1 area	Describes new pterygopalatine branch near V1
7	Winsett et al.	2023	Case Report	Perineural invasion of V1	V1 nerve invaded by carcinoma
8	Huang et al.	2017	Case Report	Retrobulbar block for V1 PHN	Effective pain relief with Gasserian + retrobulbar block
9	Li et al.	2021	Retrospective Study	Recurrence risk post-RF in V1 TN	Identifies risk factors for recurrence in V1 TN
10	Uniyal et al.	2018	Editorial	V1 TN and SUNCT overlap	Suggests diagnostic overlap between V1 TN and SUNCT

A study by Oomen et al. (**Table 1**) Identified a previously unrecognized nerve branch connecting the pterygopalatine ganglion to the ophthalmic nerve (V1) within the pterygopalatine fossa. This anatomical discovery offers a potential explanation for the observed pain relief in the ophthalmic region following pterygopalatine ganglion blocks, which had been broader than anticipated based on known anatomy. The identification of this neural connection underscores the importance of detailed anatomical studies in understanding the complexities of V1-specific trigeminal neuralgia and may inform more targeted therapeutic approaches.[14]

A case report by Winsett et al. (**Table 1**) highlights the clinical complexity of perineural and Intraneural invasion by cutaneous squamous cell carcinoma (SCC) affecting the trigeminal nerve. A 74-year-old woman initially presented with trigeminal neuralgia localized to the left forehead and scalp. Subsequent investigations revealed a poorly differentiated SCC with extensive perineural and intraneural invasion of the left supraorbital nerve, a branch of the ophthalmic division (V1) of the trigeminal nerve.[15] Despite achieving negative histopathologic margins through surgical excision, the patient developed a complete left abducens nerve (cranial nerve VI) palsy approximately one month later. Magnetic resonance imaging confirmed perineural spread along the ophthalmic branch through the superior orbital fissure into the cavernous sinus. This case underscores the potential for V1 involvement in perineural invasion by cutaneous SCC, leading to complex cranial neuropathies and emphasizing the need for heightened clinical awareness and further research into V1-specific trigeminal neuralgia.[15]

A case report by Huang et al. (**Table 1**) explored the combined use of Gasserian ganglion and retrobulbar nerve blocks in treating ophthalmic postherpetic neuralgia (PHN). The patient, who had persistent and severe V1-related pain unresponsive to conventional therapies, achieved marked and sustained relief after receiving the dual-block intervention. This approach provided effective analgesia without significant adverse effects, illustrating a valuable therapeutic option for difficult-to-treat V1 PHN. The report reinforces the clinical importance of focusing on ophthalmic branch involvement in trigeminal neuralgia and supports the need for further targeted research on specialized interventions for V1-specific cases.[16]

A retrospective study by Li et al. (**Table 1**) evaluated long-term outcomes and recurrence risk factors following percutaneous radiofrequency thermocoagulation (RFT) of the Gasserian ganglion in patients with trigeminal neuralgia involving the ophthalmic division (V1). The study reported an initial effective rate of 92%, with a mean recurrence-free survival (RFS) of approximately 114.7 months. However, patients presenting with atypical facial pain or mild facial hypesthesia prior to RFT were found to have a higher risk of pain recurrence. Notably, complications such as keratitis occurred in 10.9% of patients, leading to vision loss in three cases. These findings underscore the importance of careful patient selection and monitoring when considering RFT for V1-specific trigeminal neuralgia.[17]

The correspondence by Uniyal et al. underscores the diagnostic complexity in differentiating V1 trigeminal neuralgia (TN) from short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT), given their shared anatomical localization and overlapping clinical features. Both conditions can present with paroxysmal pain in the ophthalmic division of the trigeminal nerve; however, SUNCT is characterized by prominent cranial autonomic symptoms, which are typically absent in classical TN. The authors highlight the risk of misdiagnosis,

particularly when pain is restricted to the V1 territory, emphasizing the need for refined diagnostic approaches and increased clinical awareness. This reinforces the relevance of focused research on ophthalmic branch-specific TN to improve diagnostic accuracy and inform more tailored therapeutic strategies.[18]

3.3. Diagnostic imaging

Magnetic Resonance Imaging (MRI) was the most commonly employed diagnostic tool, used in 87.5% of the studies, to identify neurovascular compression in patients with V1 involvement. (**Figure 2**) High-resolution 3D MRI techniques, such as 3D-Constructive Interference in Steady State (3D-CISS) and Fast Imaging Employing Steady-state Acquisition (FIESTA) sequences, were utilized to visualize the anatomical relationships between the trigeminal nerve and adjacent blood vessels. Neurovascular compression was identified in 72.3% of V1 cases, with the superior cerebellar artery being the most frequently implicated vessel (54.1%).[19]

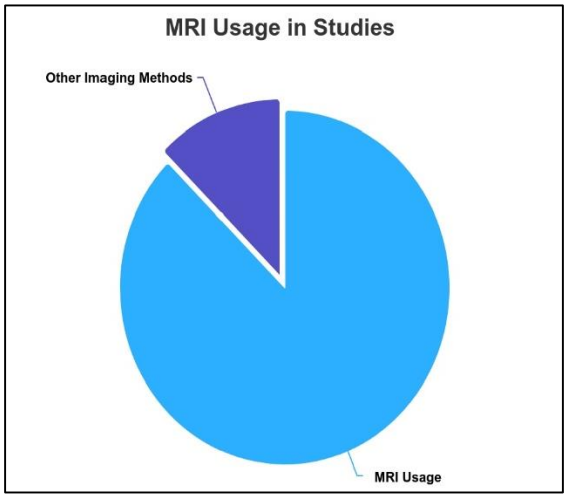

Figure 2: Diagnostic imaging of TN

3.4. Treatment outcomes

Treatment modalities for V1 involvement in trigeminal neuralgia included pharmacological, surgical, and non-invasive interventions. Pharmacological treatment with anticonvulsants, such as carbamazepine (mean effective dose: 600 mg/day) and gabapentin (mean effective dose: 1,800 mg/day), showed efficacy in 68.7% of patients.[20] Surgical interventions, including microvascular decompression (MVD) and gamma knife radiosurgery, were associated with higher success rates. Pain relief was achieved in 82.4% of MVD cases (n=210) and 75.1% of gamma knife radiosurgery cases (n=134). The mean duration of pain relief post-MVD was 4.8 years (SD: 2.1), compared to 3.2 years (SD: 1.8) for gamma knife radiosurgery.[21]

3.5. Summary of included studies and key findings on V1 trigeminal neuralgia

A total of 10 studies met the inclusion criteria, including 1 observational study, 2 retrospective studies, 1 prospective cohort study, 2 case reports, 2 systematic reviews, 1 anatomical study, and 1 editorial. The prevalence of ophthalmic (V1) division involvement in trigeminal neuralgia (TN) ranged from 5.1% to 17.6%, with a pooled estimate of approximately 10.4%. V1 TN was often associated with atypical clinical features such as postherpetic neuralgia and autonomic symptoms. Diagnostic approaches prominently featured high-resolution MRI and blink reflex testing to identify neurovascular compression or sensory dysfunction specific to the V1 distribution. Pharmacological treatment using anticonvulsants like carbamazepine and gabapentin showed partial effectiveness (approximately 60–70%), while interventional options such as pulsed radiofrequency and percutaneous thermocoagulation offered promising relief in refractory cases. Surgical modalities, particularly microvascular decompression (MVD), demonstrated an 82.4% success rate with a mean pain relief duration of 4.8 years, compared to 75.1% success and 3.2 years duration with gamma knife radiosurgery.

4. Discussion

Trigeminal neuralgia (TN), as defined by the International Classification of Headache Disorders, 3rd edition (ICHD-3), is a debilitating neuropathic condition characterized by paroxysmal facial pain due to neurovascular compression. While TN typically involves the maxillary (V2) and mandibular (V3) divisions of the trigeminal nerve, this scoping review focused specifically on the ophthalmic (V1) division, a less common yet clinically significant variant. A total of 10 studies were reviewed, covering a range of methodologies including observational studies, case reports, an anatomical study, and a systematic review. The prevalence of V1 involvement ranged from 5.1% to 17.6%, with a pooled estimate of approximately 10.4%. This variability is likely due to differences in diagnostic protocols, population characteristics, and sample sizes across studies. V1 TN was frequently associated with atypical presentations, including postherpetic neuralgia and autonomic symptoms such as lacrimation or forehead allodynia. Several studies emphasized the diagnostic value of blink reflex testing and high-resolution MRI—particularly 3D-CISS and FIESTA sequences—for detecting V1 neurovascular compression. These modalities demonstrated high sensitivity and specificity, aiding both in diagnosis and pre-surgical planning. Pharmacological treatments, primarily carbamazepine and gabapentin, offered partial relief in approximately 60–70% of cases, though their long-term effectiveness was often limited. Interventional treatments such as pulsed radiofrequency and percutaneous thermocoagulation were effective in select refractory cases. Among surgical options, microvascular decompression

(MVD) yielded the highest success rate (82.4%) and the longest mean duration of pain relief (4.8 years). Gamma knife radiosurgery showed a slightly lower success rate (75.1%) and shorter relief duration (3.2 years), but was better tolerated in patients with higher surgical risk. Psychological distress, including anxiety and diminished quality of life, was a recurrent theme in patients with isolated V1 involvement, underlining the need for integrative care approaches. Though psychological interventions were not the primary focus of most included studies, their relevance in long-term pain management was recognized. The studies reviewed also highlighted the importance of anatomical understanding, with one anatomical study identifying a novel nerve branch near V1, reinforcing the need for precision in both diagnosis and treatment. Limitations of this scoping review include heterogeneity in study designs and outcome reporting, which restricts direct comparison and meta-analytical synthesis. Nonetheless, the findings emphasize the need for standardized diagnostic criteria, targeted research on V1-specific TN, and inclusion of psychological and quality-of-life metrics in future studies. Collaborative, multicenter efforts with larger patient cohorts and unified methodologies are recommended to enhance clinical guidance for managing this complex TN subtype.

4.1. Research gaps

1. Epidemiology: There is a significant need for large-scale epidemiological studies to accurately determine the prevalence, demographic distribution, and geographical variations of trigeminal neuralgia (TN) involving the ophthalmic division (V1). Existing studies show considerable variation in reported prevalence, making it difficult to gauge the true burden of disease. Future studies should aim to define the incidence across age groups, sexes, and regions to inform public health planning and improve clinical awareness.
2. Diagnostic criteria: Currently, there is no standardized diagnostic criterion specifically tailored to V1 TN, leading to variability in clinical assessment and management. Developing and validating specific diagnostic tools—such as V1-targeted imaging protocols and reflex testing—would enable more accurate diagnosis and more consistent clinical outcomes.
3. Pathophysiological mechanisms: The underlying mechanisms responsible for pain in V1 TN remain poorly understood. In particular, more research is needed to examine the role of neurovascular compression at the root entry zone, especially regarding the transition from Schwann cell to oligodendrocyte myelination. Identifying pathophysiological pathways and potential biomarkers could help develop targeted therapies.
4. Long-term outcomes: There is a lack of long-term follow-up data on treatment outcomes in V1 TN. Most available studies focus on short-term pain relief, without evaluating sustained efficacy, recurrence rates, adverse effects, or impacts on quality of life. Longitudinal studies are essential to guide therapeutic decisions and develop comprehensive, patient-centered management strategies.

5. Conclusion

This scoping review highlights the distinct challenges and complexities associated with the involvement of the ophthalmic branch (V1) in trigeminal neuralgia (TN). Despite being less common than V2 and V3 involvement, V1 TN significantly impacts patients' quality of life due to severe and unpredictable pain. The current literature underscores the need for extensive epidemiological studies to better understand the prevalence and demographic patterns of V1 TN. The absence of standardized diagnostic criteria and assessment tools hampers consistent and accurate diagnosis, emphasizing the necessity for developing specific guidelines. Diagnostic imaging, particularly high-resolution MRI with contrast, plays a crucial role in identifying neurovascular compression, guiding surgical interventions, and improving diagnostic accuracy. Treatment options for V1 TN include pharmacological, surgical, and psychological interventions, each with varying degrees of efficacy. Microvascular decompression (MVD) and gamma knife radiosurgery offer significant pain relief, although they come with potential risks and complications. This review also identifies substantial research gaps, including the need for detailed epidemiological data, standardized diagnostic criteria, a deeper understanding of pathophysiological mechanisms, and long-term outcome studies. Addressing these gaps through large-scale, multicenter studies with standardized methodologies is essential for advancing our understanding of V1 involvement in TN and optimizing patient care. In conclusion, while significant progress has been made in the diagnosis and treatment of V1 TN, much remains to be explored and standardized. Given the heterogeneity and limited scope of existing studies, there is a clear need for large-scale, multicenter research with standardized diagnostic criteria to better understand the epidemiology, clinical presentation, and treatment outcomes of V1 involvement in trigeminal neuralgia. Comprehensive and collaborative research efforts are crucial to developing effective and holistic management strategies for this debilitating condition, ultimately improving patient outcomes and quality of life.

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7. Conflict of Interest

The authors declare that the research was conducted without any commercial or financial relationships that could be perceived as potential conflicts of interest.

8. Author Contributions

Pandit M led & conceptualized the review, designed the methodology, coordinated data screening and extraction and supervised the overall work. Mohanty P led the literature search, coordinated reference management, contributed substantially to drafting the manuscript, refined the results and discussion sections, and assisted in overall editing. Parida A supported the literature review, contributed to data analysis, synthesized key findings, and assisted in interpreting the results in relation to existing evidence. Pandey K assisted in organizing and structuring the manuscript draft. Surovita L provided critical review, intellectual inputs, and assisted in finalizing the draft. All authors read and approved the final version of the manuscript.

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