### ACUTE PAIN MEDICINE (R URMAN, SECTION EDITOR)



# Modern Approaches to the Treatment of Acute Facial Pain

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# Abstract

**Purpose of Review** Acute facial pain presents a complex challenge in medical practice, requiring a comprehensive and interdisciplinary approach to its management. This narrative review explores the contemporary landscape of treating acute facial pain, delving into pharmacological, non-pharmacological, and advanced interventions. The significance of tailored treatment strategies, rooted in the diverse etiologies of facial pain, such as dental infections, trigeminal neuralgia, temporomandibular joint disorders, sinusitis, or neurological conditions like migraines or cluster headaches, is underscored. We particularly emphasize recent advances in treating trigeminal neuralgia, elucidating current treatment concepts in managing this particular acute facial pain.

**Recent Findings** Recent research sheds light on various treatment modalities for acute facial pain. Pharmacotherapy ranges from traditional NSAIDs and analgesics to anticonvulsants and antidepressants. Non-pharmacological interventions, including physical therapy and psychological approaches, play pivotal roles. Advanced interventions, such as nerve blocks and surgical procedures, are considered in cases of treatment resistance. Moreover, we explore innovative technologies like neuromodulation techniques and personalized medicine, offering promising avenues for optimizing treatment outcomes in acute facial pain management.

**Summary** Modern management of acute facial pain requires a nuanced and patient-centric approach. Tailoring treatment strategies to the individual's underlying condition is paramount. While pharmacotherapy remains a cornerstone, the integration of non-pharmacological interventions is essential for comprehensive care. Advanced interventions should be reserved for cases where conservative measures prove inadequate. Furthermore, leveraging innovative technologies and personalized medicine holds promise for enhancing treatment efficacy. Ultimately, a holistic approach that considers the diverse needs of patients is crucial for effectively addressing acute facial pain.

Keywords Acute pain; facial · Medical treatment · Intervention · Surgery

# Introduction

The underlying causes of acute facial pain are diverse, encompassing conditions such as dental infections, trigeminal neuralgia (TN), temporomandibular joint disorders,

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<sup>1</sup> Department of Neurosurgery, Cantonal Hospital of Aarau, Aarau, Switzerland sinusitis, migraines, and cluster headaches (Fig. 1)  $[1^{\bullet}, 2^{\bullet}, 3-5]$ .

As such, effective management of acute facial pain in contemporary medicine necessitates a holistic approach that draws upon various specialized disciplines. Collaborative

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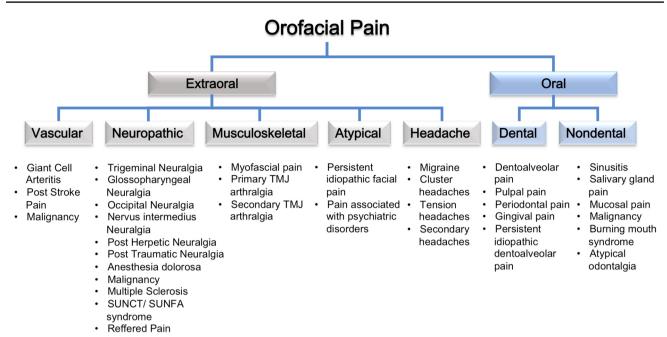


Fig. 1 The differential diagnosis of facial pain encompasses various possibilities. Extraoral facial pain may arise from neuropathic disorders, vascular disorders, temporomandibular disorders, or atypical

efforts spanning neurology, otolaryngology, neurosurgery, dentistry, and anesthesiological pain management are integral to address this complex condition comprehensively  $[2\bullet, 5,$ 6]. Consequently, treatment protocols must be meticulously customized to address the specific underlying etiology of the pain  $[1 \bullet, 2 \bullet, 7 - 9]$ . The cornerstone of this approach lies in the utilization of both pharmacological and non-pharmacological interventions. Pharmacotherapy comprises a range of options, including nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, muscle relaxants, anticonvulsants, or antidepressants, tailored to the specific diagnosis and characteristics of the pain [10, 11]. Simultaneously, non-pharmacological interventions encompass physical therapy, acupuncture, chiropractic manipulation, and psychological approaches like cognitive-behavioral therapy (CBT), which can be initiated in the acute phase to identify and address associated anxiety or depression promptly [12–15]. When conservative measures prove insufficient in providing relief, advanced interventions merit consideration. These encompass nerve blocks, botulinum toxin injections, radiofrequency ablation, with microvascular decompression being particularly notable for conditions like trigeminal neuralgia (TN) [16, 17]. In recent years, the latter has gained prominence as a first-line treatment due to its high success rates and durable outcomes, even when neurovascular conflict is absent, provided that other underlying causes, such as tumors or multiple sclerosis lesions in the brainstem nucleus of the trigeminal nerve contributing to secondary TN, have been ruled out [18, 19••, 20••]. Additionally, advancements in medical technology have led to the development of innovative

causes. Pain originating from within the mouth can be attributed to dental or nondental causes. Abbr.: TMJ, temporomandibular joint

approaches for managing acute facial pain. Neuromodulation techniques such as transcutaneous electrical nerve stimulation (TENS) or peripheral nerve stimulation (PNS) can offer targeted pain relief with minimal side effects, although they are not used as primary treatment for acute pain symptoms [15, 17, 21]. Furthermore, the emergence of personalized medicine and precision diagnostics holds promise for optimizing treatment outcomes in patients with acute facial pain. By utilizing genetic testing, imaging modalities, and other biomarkers, clinicians can better tailor treatment approaches to individual patients, improving efficacy and minimizing adverse effects [6].

In this narrative review, we describe the intricate landscape of managing acute facial pain, stressing the importance of a comprehensive, interdisciplinary approach that encompasses various causes. In particular, we delve into modern treatment modalities, encompassing pharmacological, non-pharmacological, and advanced interventions, with particular attention to recent developments in addressing TN as a significant component in the array of acute facial pain disorders.

# Pharmacologic Treatments for Trigeminal Neuralgia

Treatment for TN includes pharmaceutical interventions, surgical procedures, and complementary methods [15,  $20 \bullet \bullet$ ], with anti-epileptic drugs typically utilized as the

first-line treatment, [5, 16, 17, 22, 23] while secondary TN should be treated for underlying pathologies [5, 23]. Primary pharmacological options in initial therapy include sodiumblocking agents such as carbamazepine and oxcarbazepine, while lamotrigine, gabapentin, and baclofen are among the secondary options [16, 17, 23]. Sodium-blocking agents, notably carbamazepine, typically demonstrate superior efficacy in addressing paroxysmal firing. Conversely, gabapentinoids and antidepressants have shown effectiveness in managing persistent pain [17]. These alternative treatments can be employed independently or alongside other therapies as supplements [24, 81].

### Carbamazepine and Oxcarbazepine

Carbamazepine and oxcarbazepine, the latter being a structural keto derivative of the former, find extensive application in addressing a wide range of neuropathic pain conditions [16, 25]. Both medications extensively diminish the occurrence and severity of painful episodes, exhibiting equal efficacy in alleviating both spontaneous and trigger-induced attacks. Consequently, they provide significant initial pain relief to nearly 90% of patients [25, 26••, 27]. However, both drugs have a serious side effect profile, including hyponatremia, drug-drug interactions, aplastic anemia, and liver failure [20••]. Nevertheless, due to the high success in initial pain control, they remain the most effective medications, especially in the early stages of TN [28, 29]. In a comprehensive investigation involving typical instances of TN displaying resistance to carbamazepine treatment, it was observed that monotherapy with oxcarbazepine yielded additional pain alleviation in 37.1% of cases [30]. This finding suggests that oxcarbazepine holds promise as a viable recourse for patients encountering ineffectiveness with carbamazepine therapy, serving as a potential salvage strategy for those who do not derive relief from the standard treatment  $[20 \bullet \bullet]$ . It is crucial to note that while many patients initially respond to first-line therapy, most treatment approaches tend to diminish in efficacy over time, highlighting the need for new and innovative treatment options [31].

### Lamotrigine and Baclofen and Gabapentin

For TN patients who are intolerant of, or have contraindications to first line therapies, baclofen, lamotrigine or gabapentin are frequently viable alternatives [17, 20••, 28]. Moreover, patients who do not respond to first-line carbamazepine monotherapy have demonstrated potential benefits from combination therapy [20••, 32]. Nevertheless, there is a lack of randomized controlled trials directly comparing the efficacy of monotherapy against combination therapy in treating TN [28]. Each of these second line therapies come with certain pitfalls. Baclofen, a GABA<sub>B</sub> receptor agonist, reduces the number of painful episodes and prolongs remission [20••]. The adverse effects of baclofen within a therapeutic window of up to 80 mg/day encompass drowsiness, muscle weakness, fatigue, and cognitive deficits. Additionally, the narrow therapeutic range of baclofen necessitates vigilant monitoring during dose initiation, with tapering recommended [20••, 33]. The effectiveness of baclofen is constrained by these adverse effects, often hindering the administration of an adequate oral dose required for meaningful pain alleviation [29]. Lamotrigine is an anticonvulsant that inhibits glutamate release by blocking voltage-gated sodium channels [20••, 24]. Within a therapeutic dosage range of up to 600 mg/day, its adverse effects may include sleepiness, dizziness, headache, vertigo, and ataxia [20••, 28, 34]. However, evidence supporting its efficacy is generally low [10, 34]. Gabapentin, an anticonvulsant designed to mimic the neurotransmitter GABA, lacks clear evidence regarding its effectiveness as monotherapy [20••]. A recent comprehensive examination involving a systematic review and meta-analysis, which scrutinized 18 randomized controlled trials, confirmed the efficacy and enhanced tolerability of this treatment in contrast to carbamazepine. However, the overall quality of the studies included in the analysis was deemed insufficient [35]. Due to the scarcity of evidence, it is understandable that some experts recommend early surgical referrals for patients unresponsive to first-line therapy, as they are less likely to respond to alternative medications for trigeminal neuralgia [28, 29].

## **Alternative Pharmacotherapy**

Several other drugs have demonstrated some evidence of efficacy for TN as well as other causes of acute facial pain in small, generally lower-quality controlled trials [28]. These include medications like pregabalin, pimozide, topical lidocaine, clonazepam, misoprostol, valproate, and others [11,  $20 \cdot 0.34$ ]. However, due to a lack of longitudinal data, the long-term efficacy of these drugs still remains unknown.

## Analgesics

Many current treatment strategies prioritize long-term symptom management but often overlook the immediate relief of acute facial pain episodes. Rapid pain alleviation is essential for sudden and severe exacerbations of facial pain. Current recommendations advocate for the use of local anesthetics, particularly lidocaine (applied ophthalmically, intranasally, orally, via trigger point injection, administered intravenously, or utilized for nerve blocks), anticonvulsants (such as phenytoin or its derivative, fosphenytoin), and serotonin agonists (administered subcutaneously or intranasally, such as sumatriptan) [10, 36, 37].

# **Botulinum Toxin Injections**

Botulinum neurotoxin stands as a potent biological toxin and a formidable therapeutic agent, finding broadening utility across an expanding spectrum of clinical applications within the orofacial domain [38]. Its efficacy is particularly pronounced in addressing movement disorders, regulating saliva secretion, and managing both acute and neuropathic pain [39, 40]. Botulinum toxin exerts its pain-relieving effects through various mechanisms, including the reduction of inflammation, deactivation of sodium channels, and inhibition of axonal transport junctions [20••]. It has emerged as a novel and promising alternative to surgery for individuals whose pain is unresponsive to medication [41]. A recent systematic review and meta-analysis highlighted four small placebo-controlled randomized controlled trials assessing the use of botulinum toxin A for TN. The overall effect demonstrated an 85% reduction in TN attacks [42]. Botulinum toxin injections hold potential benefits for patients with TN and other orofacial disorders, although data remain limited at present.

# Interventional Treatments for Trigeminal Neuralgia

While medication currently stands as the primary approach for managing acute facial pain, [22, 23] prolonged pharmaceutical pain management presents drawbacks, as longterm usage is associated with various side effects [43].

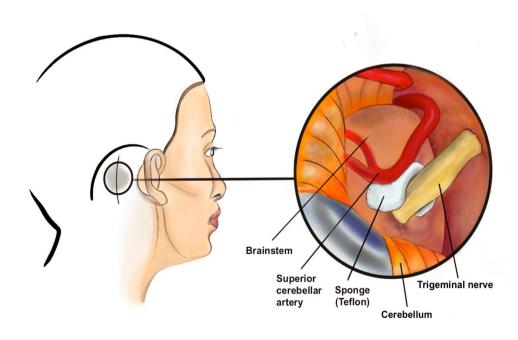
**Fig. 2** Microvascular decompression for TN. Retromastoid craniotomy is performed through a small incision behind the ear. Small pads of Teflon are placed between the trigeminal nerve and the artery (i.e. superior cerebellar artery) to decompress the nerve and preserve its normal function

Consequently, surgical intervention becomes a consideration when drug therapy proves ineffective or leads to intolerable side effects [22, 44, 45]. The European Academy of Neurology guidelines recommend medical management with appropriate doses and regular monitoring before considering surgery [17, 46•]. However, the optimal number of drugs before surgical referral has not yet been determined [47].

#### **Microvascular Decompression**

Microvascular decompression (MVD) surgery stands as a well-established and effective treatment option for TN, intermedius neuralgia, hemifacial spasm, and glossopharyngeal neuralgia [18, 19••, 48]. After Peter J. Jannetta reported promising results for MVD surgery in 1996, [49] it has become the surgical treatment of choice for TN. MVD is considered the primary surgical option and the only treatment addressing the etiology of classical TN [50, 51]. This surgical intervention tackles the challenge of vascular compression, which constitutes 85% of TN cases [19••].

For MVD, the retrosigmoid approach with a 3–4 cm surgical incision behind the ear and a 1.5–2 cm bone window is typically considered (Fig. 2) [50]. After opening the dura mater, cerebrospinal fluid is released, allowing for gentle retraction of the cerebellum to enhance visibility at the surgical site. Following this, the responsible blood vessels, typically the superior cerebellar artery, and the trigeminal nerve at its root entry zone are separated using Teflon (see Fig. 2) or, less commonly, a sling technique [50, 52–54]. Alternatively, transposition for MVD is an elegant way of solving vessel-nerve conflicts at the cerebellopontine angle,



although a significant difference to interposition could not be proven [55].

Outcomes following MVD are generally positive, with systematic reviews indicating success rates exceeding 90% for the initial surgical treatment [51, 56–58]. Research suggests that patients who undergo MVD experience favorable long-term pain control outcomes, with approximately 70% of individuals becoming pain-free and no longer requiring medication a decade post-surgery [20••]. Moreover, those who undergo early MVD treatment express greater satisfaction compared to those opting for drug therapy [50, 59]. The recurrence rate ranges from 14 to 16% [44, 50, 59]. Although complications such as facial numbness, dull sensation, and vertigo are not uncommon, more severe complications like cerebral infarction, facial paralysis, hearing impairment, and infection are rare, occurring in less than 3% of cases [43, 56]. Full endoscopic vascular decompression has been suggested as a substitute for traditional MVD, providing similar therapeutic benefits with minimized surgical trauma, enhanced visibility of the surgical field, and potentially lower incidences of recurrence and complications [60]. However, the findings regarding its efficacy are varied.

### **Percutaneous Balloon Compression**

In recent year, percutaneous balloon compression (PBC) has emerged as a valuable therapeutic option in the management of TN [61-63]. This minimally invasive procedure is indicated for patients who have failed to respond to conservative treatments or are not suitable candidates for more invasive surgical interventions  $[20 \bullet , 62, 64]$ . Despite its poential association with nerve damage, it has been demonstrated that the therapeutic efficacy of PBC may be comparable to that of MVD, [62, 65] yet the long-term results are less favorable [66]. The surgery involves inserting a small catheter through the patient's cheek to access the Gasserian ganglion, either under fluoroscopic guidance or neuronavigation. Once the catheter is properly positioned, a small balloon is inflated to compress the trigeminal nerve, aiming to disrupt the abnormal pain signals responsible for TN [62, 64]. Studies have reported varying success rates with PBC, ranging from 80 to 90% in achieving pain relief and time free from medications from 2 to 3 years [63]. Recent studies demonstrate pain recurrence between 15 and 50% over 2-5 years [ $20 \bullet \bullet$ , 67]. Various factors have been identified as having an impact on the results of balloon compression. These factors encompass the shape of the inflated balloon, the pressure at which the balloon opens, the quantity of contrast injected, the duration of compression, and the specific underlying medical condition being treated [68, 69]. Of note, the procedure may result in facial sensations, cranial nerve deficits, and sudden heart rate changes due to trigeminal cardiac reflexes, although such occurrences are rare  $[20 \bullet \bullet,$  69]. Nevertheless, compared to MVD, PBC offers shorter operation times, lower anesthesia risks, and the possibility of repeated procedures [61]. Nonetheless, it is noteworthy that there exists a notable incidence of trigeminal motor function impairment (66%), frequently prompting the need for repeated interventions owing to the heightened recurrence propensity [50, 64].

### **Percutaneous Glycerol Infiltration**

Percutaneous glycerol infiltration (PGC) or glycerol rhizotomy, is an alternative minimally invasive procedure used in the management of TN [19••, 20••]. Like for PBC, the primary indication is for patients who have not achieved sufficient relief from pharmacological treatments or who are not suitable candidates for MVD surgery  $[20 \bullet , 64]$ . Thereby, glycerol acts by damaging the trigeminal nerve fibers interrupting the abnormal pain signals responsible for TN [64]. Recent results indicate that glycerol rhizotomy displays a high short-term success rate, with over 90% of patients obtaining initial relief and over 50% of patients remaining pain free at three years [22]. However, MVD typically provides better and longer-lasting pain relief compared to percutaneous surgery, despite an increased risk of complications [70]. Balloon compression among percutaneous procedures offers the most durable pain relief [70]. Factors such as older age and post-operative numbness predict favorable outcomes from percutaneous surgery [70]. Currently, these findings can aid clinicians in the decision making to guide patients with primary TN regarding neurosurgical treatment choices for acute pain management.

### **Radiofrequency Ablation**

Although primarily employed for neuropathic facial pain, radiofrequency ablation (RF) utilizes thermocoagulation to selectively deactivate pain fibers [71, 72]. Conversely, RF has also been indicated and primarily utilized for urgent management when MVD is unsuitable for the patient [72]. Thereby, various RF techniques, such as conventional RF (CRF) and pulsed RF (PRF), differ in their mechanisms and efficacy in treating acute facial pain [17]. CRF produces an electric field of 5 to 15 mm, elevating tissue temperature above 45 °C, leading to localized damage and loss of nerve fibers, while PRF administers 20 ms pulses every 0.5 s, allowing for heat dissipation, thus avoiding temperatures exceeding 45 °C [17, 73]. Consequently, PRF inflicts less harm on surrounding tissues. For optimal outcomes and safety during RF ablation at the Gasserian ganglion, the triangular plexus, extending from the posterior margin of the ganglion to the path above the upper petrous ridge, proves to be the most advantageous site for generating precise lesions [17, 74]. Nevertheless, expected complications from RF ablation include pain recurrence, diminished corneal sensation, masseter weakness, dysesthesia, and other neurological issues [72]. A very recent review analyzing 1146 patients across 13 trials have demonstrated a success rate of 89.2% with RF ablation for TN [75]. While RF is superior to glycerol rhizotomy for immediate pain relief, it poses a higher risk of pain recurrence compared to MVD [76]. Despite its effectiveness in providing complete pain relief, particularly for high-risk surgical patients, evidence regarding the safety of RF ablation remains insufficient [17]. Yet, further research is warranted to conclusively establish the safety profile.

# Stereotactic Radiosurgery and Emerging Non-invasive Therapies

Although stereotactic radiosurgery (SRS) is not recommended for the immediate management of acute pain in TN, it can be employed as a supplementary therapy subsequent to the aforementioned procedures to prolong the efficacy, particularly in patients at elevated risk of recurrence or those considered unsuitable candidates for high-risk surgery [18, 77]. This procedure, conducted on an outpatient basis, entails administering high doses of radiation, reaching up to 80 Gy, through precise targeting of submillimeter radiation beams at the trigeminal root entry zone located in the posterior fossa [25, 78]. Over time, the targeted radiation induces necrosis, consequently diminishing pain signals [51]. Thereby, the most frequent complications reported are paraesthesias and facial numbress [51]. The literature is limited in its level of evidence, with only one comparative randomized trial [79]. A systematic review has illustrated a success rate of 69% at 1 year and 52% at 3 years post-surgery [22, 24, 51]. Overall outcomes were superior following MVD than following SRS, additionally a significantly higher amount stay without medication after MVD than after SRS [45]. Therefore, SRS is rarely utilized in the management of acute facial pain. In cases where the pain leans towards neuropathic pain, the utilization of deep brain stimulation has been documented to provide effective pain relief in 75-100% of patients undergoing treatment for neuropathic pain syndrome [22, 80]. However, two randomized controlled trials (RCTs) have failed due to study heterogeneity, suggesting that other less invasive methods are more promising [21, 22, 80].

Neuromodulation methods like transcutaneous electrical nerve stimulation (TENS) or peripheral nerve stimulation (PNS) present opportunities for precise pain relief with minimal adverse effects. However, they are typically employed as adjunctive rather than primary treatments for acute pain symptoms [15, 17, 21]. Moreover, the advancement of personalized medicine and precision diagnostics offers potential for enhancing treatment outcomes in individuals experiencing acute facial pain. Through the utilization of genetic testing, imaging techniques, and various biomarkers, healthcare professionals can customize treatment strategies to suit each patient's unique needs, thereby enhancing effectiveness and reducing unwanted effects [6].

In summary, the management of acute facial pain requires a comprehensive interdisciplinary approach, drawing upon various specialized disciplines. Treatment protocols must be meticulously customized to address the specific underlying etiology of the pain, utilizing both pharmacological and non-pharmacological interventions.

While pharmacological treatments such as carbamazepine and oxcarbazepine are available for trigeminal neuralgia (TN), advanced interventions like percutaneous balloon compression (PBC) and radiofrequency (RF) procedures present alternative options with differing effectiveness and safety characteristics, underscoring the need for additional research to establish definitive evidence [69]. Furthermore, MVD surgery represents a well-established and effective treatment option for TN, boasting high success rates and durable outcomes. However, it is essential to consider that multimorbid patients may not derive the same benefits from this option due to the potential perioperative complication rate. Neuromodulation techniques like TENS or PNS provide targeted pain relief, although not as primary treatments for acute pain, while personalized medicine and precision diagnostics are hypothesized to show promise in further optimizing treatment outcomes for acute facial pain through tailored interventions using genetic testing, imaging, and biomarkers.

# Conclusion

Modern approaches in treating acute facial pain encompass a comprehensive and interdisciplinary approach that integrates pharmacological, non-pharmacological, and advanced interventions. By addressing the underlying cause of the pain and utilizing a personalized treatment strategy, clinicians can effectively alleviate symptoms and improve the quality of life for patients experiencing acute facial pain.

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