

A Narrative Review of Therapeutic Peripheral Nerve Blocks for Chronic Orofacial Pain Conditions

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Submitted May 14, 2021; accepted
September 14, 2021.
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Aims: To provide an analysis of the different therapeutic peripheral nerve blocks (PNBs), as well as their limitations and the related evidence base for their use in chronic orofacial pain (OFP) conditions, excluding migraine and other headache conditions. **Methods/Results:** The evidence base for therapeutic PNBs for chronic OFP is poor and highlights the need for improved research in this area. The diagnostic criteria and interventional PNB definitions and techniques varied between studies. In addition, the placebo effect of a peripheral injection and its resultant bias was rarely considered. Most of the PNB interventions for temporomandibular disorders were for arthrogenous disorders (arthritis and disc entrapment with pain). However, there is emerging evidence for the use of onabotulinum toxin (BTX-A) in trigeminal neuralgia, with four prospective randomized controlled trials (pRCTs), and for postherpetic neuralgia. However, despite high-level evidence for BTX-A in posttraumatic neuropathic pain outside the trigeminal system, there is no evidence for its use for PTNP within the trigeminal system. **Conclusion:** There may be emerging evidence for treating trigeminal neuralgia with BTX-A injections; however, there is a need for future clinical studies of therapeutic PNBs in orofacial pain conditions. *J Oral Facial Pain Headache* 2022;36:49–58. doi: 10.11607/ofph.3017

Keywords: reversible peripheral nerve block, therapeutic nerve block, therapeutic nerve injections, trigeminal nerve block, trigeminal nerve injections

The management of orofacial pain (OFP) is challenging¹ not only due to the complexity of the anatomical region, but also due to the plethora of conditions that can affect the various tissues and the many specialists who can be involved in the patient's care. Importantly, the recent subcategorization of OFPH conditions by the International Classification of Orofacial Pain (ICOP) must be acknowledged, including: acute dental structure pain (temporomandibular disorders [TMDs]); neuropathic pain (trigeminal posttraumatic neuropathic pain [PTNP], postherpetic neuralgia [PHN], and trigeminal neuralgia [TN]); neurovascular pain (headaches affecting maxillary and mandibular divisions of the trigeminal nerve [ie, migraine, cluster headaches]); and idiopathic pain (burning mouth syndrome [BMS] or persistent facial or intraoral/dentoalveolar pain [PIFP and PDAP] conditions).²

Currently, systemic medications are the mainstay of therapy for patients with chronic OFP.³ However, their efficacy is poor, often due to the undesirable medical side effects impacting the patient's medical compliance.⁴ Psychologic interventions are increasingly gaining evidence, as clinicians are recognizing the significant impact of Axis II on the patient's presentation and behavior.⁵ Surgery is effective in classical TN,⁶ but ineffective for PTNP in nerve injury,⁷ and other interventions such as therapeutic injections of onabotulinum toxin (BTX-A) are also increasing in evidence of effectiveness for PTNP and for PHN outside the trigeminal system.^{8,9}

There are relatively few reports on alternative interventions—for example, non-BTX-A injections. Several types of injections are available to treat chronic pain, including subcutaneous, nerve blocks, ganglion blocks, and facet. There is, however, only limited evidence for their use in chronic OFP. In addition, the peripheral nerve block (PNB)

or regional nerve blockade is a short-term, reversible block applied to a specific peripheral sensory nerve. It usually lasts a few hours or days, with the deliberate interruption of an action potential (both transduction and/or transmission) for pain relief. Products for PNBs include local anesthetic (LA) alone or combined with other agents (for example, corticosteroids or antibiotics). The rationale for adding a corticosteroid is to prolong the analgesic effect.¹⁰ These injections may be applied in different regions, primarily specific nerves (maxillary or mandibular nerves, greater occipital nerve [GON], auriculotemporal nerve [AT], masseteric nerve [MN], or cervical nerve [CN]); nonneural specific anatomical areas (intra-articular [IA], intra-muscular [IM], sub-mucosal [SM]); or peripheral ganglia (eg, the sphenopalatine ganglion [SPG]).

Therapeutic or irreversible PNBs are neuroablative therapies, and these neurolytic blocks are a variant of the therapeutic block that aims to have a lasting therapeutic effect. They cause temporary or permanent degeneration of nerve fibers through the administration of chemicals, heat, or by freezing the nerve fibers, but are not included in this review.¹¹

The definition of PNBs is applied to block a peripheral nerve specifically, thus excluding: dry needling, acupuncture, central ganglia block injections (Gasserian ganglia and stellate ganglion [SGB]), intraspinal, and intracranial blocks. The difference between a peripheral and central nerve block (CNB) is the size of the target area and the injection site. The reason for performing a CNB is to stop a nerve from signaling back to the central nervous system. Blockades considered CNBs are the epidural, spinal, and intracranial blocks. Intracranial blocks, such as the trigeminal or Gasserian block, will bar the central ganglions.¹² PNBs may be used as diagnostic nerve blocks, therapeutic, prognostic, or preemptive nerve blocks; they distinguish themselves by their purpose. Diagnostic blocks will be used in the process of diagnosing a condition, while prognostic blocks are used to identify whether a treatment will be successful for chronic pain. They can be used presurgery or as pretherapeutic PNBs. Preemptive PNBs try to prevent subsequent, acute, presurgical, and persistent pain. They try to prevent central sensitization from happening.¹³

Most studies and meta-analyses available of LA PNBs focus on acute postsurgical pain after thorax, knee, and hip surgery. They often conclude that PNBs are not preferable to local infiltrations of analgesia.¹⁴ With regard to trigeminal pain, the literature review from Anugerah et al focuses on either specific peripheral techniques or headaches.¹⁵ Further reviews concentrated more on GON for migraines and cluster headaches,¹⁶ PNBs, and trigger point injections for headaches,¹⁷ with a recent review highlighting that

occipital PNBs have a poor prognosis for the outcome of occipital nerve stimulation in the treatment of headaches.¹⁸ A singular review of injection therapies for headaches and OFPs makes no recommendations.¹⁹

The rationale for the present review is that injections are standard treatment for treating chronic back, joint, and headache pain. Despite the lack of evidence, many clinicians use injection-based therapies for OFP conditions aside from headaches, and the evidence remains limited. The aim of this narrative review was to assess what evidence exists for PNB injection-based therapy for nonheadache orofacial pain and to evaluate its potential role based on developments in related conditions. This review aims to assess the current evidence base for therapeutic PNBs for chronic OFPs, excluding neurovascular conditions.

Materials and Methods

A search of specific search terms was made in the PubMed, Cochrane Database of Systematic Reviews, Google Scholar, Web of Science, and Scopus databases within the date range of January 1966 to 2019. The keywords used in the searches, using an English-language restriction, included trigeminal nerve, maxillary nerve, and mandibular nerve; trigeminal nerve block; trigeminal nerve injections; therapeutic nerve block; therapeutic nerve injections; and chronic, persistent, neuropathic, and nociceptive orofacial pain. The PICO (patient, intervention, comparison, outcome) questions applied for this narrative review were: patients suffering from chronic OFP as defined by ICOP (excluding acute pain, headaches, arteritis, and other neurovascular pain). The chronic OFP conditions included: neuropathic conditions (TN, PTNP, and PHN), idiopathic conditions (persistent intraoral pain, BMS, and persistent facial pain), and TMJ disorders (excluding intra-articular TMDs). The intervention selected was PNB for therapeutic effect (excluding diagnostic and ablative injections). The main comparative therapy was medical interventions, and the outcome assessed was the effectiveness in moderating pain and/or improving the patient's quality of life.

Results

Overall, there was low evidence for the use of LA or BTX-A PNBs for neuropathic OFP (TN, PTNP, and PHN), idiopathic conditions (persistent intraoral pain, BMS, and persistent facial pain), and TMJ disorders (excluding intra-articular TMDs). The evidence is reported under ICOP condition subheadings.

Temporomandibular Disorders

A recent narrative review³ reported on the use of PNBs in TMJ pain, myofascial pain, and BMS. A total of 15, 9, and 17 studies were found for each, respectively. Al-Moraissi et al²⁰ reported on a meta-analysis of interventions for arthrogenous TMDs and reported that studies on intra-articular injections using hyaluronic acid were low-quality evidence when reporting a substantially greater pain reduction than control/placebo groups. They concluded that minimally invasive interventions, such as intra-articular injections, should be applied before undertaking more invasive techniques. One study²¹ reported that an anesthetic block for the TMJ can reduce pain and therefore creates protective muscle splinting, can increase the mandibular range of motion, and can assist in providing a more manageable treatment.

Masseteric Nerve Block for Myalgia

One study of 60 patients presenting with TMD myalgia²² examined the masseteric nerve block (MNB) PNB in comparison with trigger point injections and an intraoral stabilization appliance (however, the specific appliance prescribed was not specified). This study reported that MNB injections instantly relieved the patients' pain, and the pain relief lasted for 2 weeks after the MNB. Since this is a retrospective study with less clear methods and results, better quality evidence is needed before concluding that MNB is a valuable treatment compared to standardized therapy for myalgia. This study followed after case reports showing improvement post-MNB PNB.²³

Intramuscular Masseteric Injections

Intramuscular masseteric injections have been shown to have therapeutic value. Unfortunately, the sample size of this study, which used bupivacaine as the LA agent, was very small.²⁴ Recently, a comparison between intramuscular injections with collagen vs lidocaine showed that collagen significantly decreased myofascial pain more than LA injections; however, the LA PNB still improved pain significantly more than the control group receiving a saline injection.²⁵ Unfortunately, more longer-term research is needed to add these injections to standardized treatment.

Auriculotemporal LA PNB

A separate study in 28 patients compared the auriculotemporal to intra-articular PNBs.²⁶ Bupivacaine was used and showed a significant deep mechanical and analgesic effect of auriculotemporal PNB.

Intra-articular Blocks

Intra-articular injections in the TMJs usually involve corticosteroids as a primary working agent, with LA

added to the substance. The corticosteroid agents used for TMJ injections are usually triamcinolone or dexamethasone, combined with 2% lidocaine without adrenaline. Ultrasound guidance may be required before injecting into the joint space.²⁷ There is a lack of prospective randomized controlled trials (pRCTs) assessing LA and corticosteroid intra-articular block injections for TMDs. The fact that caution is required when proceeding with repeated corticosteroid injections must be highlighted, as corticosteroids may cause bone resorption in joints; however, this has not been reported with single injections.²⁷ Overall, the evidence showed a decrease in pain after a corticosteroid PNB.^{28,29} Combining corticosteroids with an LA agent has proven to be effective in acute inflammatory states of the TMJ, such as acute disc displacement without reduction or polyarthritis disorders.^{30–32}

Corticosteroids can also be combined with hyaluronic acid and may be efficient in treating painful TMJs. However, better quality evidence is needed before adding hyaluronic acid to PNB injections.^{33–35} A study³⁶ was found comparing both agents, which established that there was no distinctive difference in pain and inflammation reduction between these substances. However, it was a placebo-controlled trial, and hyaluronic acid showed better results than the applied placebo.

The results found for the comparison of an LA agent combined with corticosteroid intra-articular injection and LA combined with hyaluronic acid intra-articular injection with placebo are mixed. Overall, intra-articular LA combined with a corticosteroid PNB had the highest success rates, followed by hyaluronic acid and then placebo, with the lowest beneficial effect on patients. In 2017, a systematic review examined intra-articular injections in the treatment of TMDs.³⁷ Their findings showed that patients suffering from TMJ osteoarthritis and undergoing arthrocentesis benefited from a corticosteroid injection to decrease the pain postinjection. The corticosteroid PNB does not favor increased mouth opening. Alternatively, these patients might gain from a combined corticosteroid–hyaluronic acid injection before considering arthrocentesis. The data showed that hyaluronic acid on its own might be more effective and safer, considering the risks of multiple corticosteroid injections. Fischhoff and Spivakovsky³ found that intra-articular injections of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and hyaluronates are potent for treating TMJ pain.

Intra-articular platelet-rich plasma (PRP) injections have also been considered. A systematic review was found for these types of injections in the treatment of TMDs. The review reported that there is minimal evidence for PRP in TMJ osteoarthritis.³⁸

Neuropathic Pain

Posttraumatic trigeminal neuropathic pain.

Submucosal injections

Most studies on submucosal injections treating PTNP use corticosteroids and BTX-A as agents.^{39,40} Recent evidence for injections with an LA agent is lacking. The available data use the LA PNB to diagnose rather than as a therapeutic treatment for chronic posttraumatic OFF.⁴¹

Occipital nerve block

A study of 20 patients reported successful pain management in cranial neuralgias using an occipital nerve block.⁴² The study included 8 patients with TN, 6 with trigeminal neuropathic pain, 5 with persistent idiopathic facial pain, and 1 with occipital neuralgia. The response was defined as having at least a 50% reduction in the original pain. The mean response rate was 55%, with the greatest efficacy in TN pain (75%) but less efficacy in trigeminal neuropathic pain (50%).

Sphenopalatine ganglion block

PTNP may be, in part, a sympathetic-mediated orofacial pain disorder. It is known that changes in the sympathetic system are linked to the development of chronic pain.⁴³ An SGB PNB could be considered; unfortunately, the evidence level for its use treating OFF conditions remains weak. A more recent review was found⁴⁴ stipulating that when an SGB PNB is performed as early as possible for an OFF condition, the continued severity of the pain will possibly be lower, and the likelihood for it to become chronic neuropathic pain will decrease compared to patients not receiving an early stage SGB. An older study⁴⁵ was included in this review that examined 17 patients with PTNP, and SGB was performed in 14 of the patients. Even though the results were relatively promising, with 10 patients withstanding a decrease of their pain for a prolonged time of 12 months, the study is of lesser quality and there is a need for further good-quality evidence.

Trigeminal Neuralgia.

TN is one of the most documented neuralgias. Several types of injections are available, and the evidence shows promise.

Mucosal lidocaine patch vs PNB

Although not an injection as such, lidocaine patches have proven their efficacy in the clinical context. A pRCT evaluated PNBs with 8% lidocaine vs medical-grade saline applied in 24 patients suffering from TN with acute outbursts and a refractory component. Interestingly, of the 24 patients, 19 described marked or moderate relief in pain after the lidocaine injection, and only 3 described the same after saline application.⁴⁶

Infraorbital block

Takechi et al retrospectively examined their database for patients with maxillary-branch TN who could not continue their drug-based treatment due to side effects caused by carbamazepine. Six patients were

included and responded well to an infraorbital PNB using the neurolytic agent tetracaine dissolved in bupivacaine.⁴⁷

Another case report⁴⁸ described successful management of TN using lidocaine as an agent for an infraorbital PNB.

Subcutaneous injections

Di Stani et al prospectively evaluated 13 TN patients.⁴⁹ These patients had only previously been treated with medication before recruitment into the study. Primarily, the researchers found statistically significant results, showing that the pain episodes were reduced in frequency. Other improved symptoms were the patient's mood and depression, pain scores, and general health. These authors tested the number of painful episodes 30 days and 90 days after the PNB injections and showed the clinical benefit of combining pharmacotherapy and LA PNBs for the treatment of TN.

The available evidence and case reports⁵⁰ seem incredible and show that some TN patients have 100% pain relief, lasting from a few days up to a longer period. A recent systematic review of rescue strategies for refractory TN reports evidence that LA, lidocaine (ophthalmic, nasal or oral mucosa, trigger point injection, intravenous infusion, or nerve block) may be beneficial used in conjunction with several medical interventions, including phenytoin or fosphenytoin (intravenous infusion), serotonin agonist, or sumatriptan (subcutaneous injection, nasal).⁵¹ A recent meta-analysis showed that lidocaine, BTX-A, and carbamazepine rose above other treatment options for refractory TN thanks to their high efficacy and could be recommended as the primary choice of treatment for TN.⁵² This meta-analysis included four pRCTs using BTX-A for trigger region injections.

GON block with LA

GON LA blocks can be very effective for certain facial pain pathologies. Jürgens et al showed that using LA injections with or without corticosteroids can be effective in craniofacial neuralgias (trigeminal neuropathies, glossopharyngeal, and occipital neuralgias). This research of 20 patients reported successful pain management in cranial neuralgias using GON PNBs.⁵³ The study included 8 patients with TN, 6 with trigeminal neuropathic pain, 5 with persistent idiopathic facial pain, and 1 with occipital neuralgia. A significant response was defined as a reduction in the original pain of at least 50%. The mean response rate was 55%, with the greatest efficacy in TN (75%) and occipital neuralgia (100%). The potency was less for patients with trigeminal neuropathic pain (50%) and persistent idiopathic facial pain (20%). In a recent case report, a patient with classical TN did not respond to the occipital nerve block.⁵⁴

SPG block with LA

A systematic review⁵⁵ included 60 articles on SPG block compared to a topical application of the sphenopalatine block in the form of a nasal spray. The nasal spray showed more significant applications, results, and higher-quality data. Some case reports showed the benefits of injecting lidocaine and bupivacaine against TN pain through an SPG. Multiple SPG LA PNBs over time seem to maintain the pain-relieving effect to a longer extent. Corticosteroids might be added through the Tx360 Nasal Applicator (Tian Medical), but, scientifically, this technique is still theoretical.^{56,57}

Postherpetic neuralgia.

PHN can be very debilitating. The neuralgia is caused due to the varicella-zoster virus being latently present in the patient's body after a primary infection. The virus then causes a relapse and induces neuropathic pain. The cause for neuropathic pain is damage to one or more peripheral branches of the trigeminal nerve.

Although PHN may be one of the indications for an SPG PNB, the qualitative evidence available only comprises the level of case reports.⁵⁸

Another case report⁵⁹ was published using a PNB of mepivacaine 2% in combination with triamcinolone 20 mg to anesthetize the infraorbital nerve. The pain before the procedure was scored as a 9 on a 0–10 visual analog scale (VAS). The results of the PNB were not successful enough for the patient, as the pain only went down to 4/10 and lasted for 2 weeks. Therefore, they went on trialing other procedures.

In a placebo-controlled pRCT, Makharita et al recruited 64 patients with PHN⁶⁰ and used a combination of bupivacaine and dexamethasone through a stellate ganglion block (SGB). The stellate ganglion carries all the sympathetic nerve A receptors that innervate the head, neck, and upper extremities. They discovered that the PHN episodes of patients receiving an SGB in combination with regular treatment for PHN were a lot shorter. Additionally, the pain perceived by these patients had gone down significantly compared to regular treatment. Therefore, the researchers concluded that it is beneficial to combine an SGB with anti-viral medication when patients experience a PHN episode.

Idiopathic OFP

Burning mouth syndrome.

LA PNBs

Several types of LA PNBs can be used for BMS. There is not much evidence to prove that SGBs can be effective for BMS. One case report⁶¹ showed significant results and loss of pain after the SGB PNB.

Lingual LA PNBs have been researched to treat pain induced by BMS. A study of 17 patients with BMS⁶² measured the BMS pain using a VAS at all

stages of the trial. The pain was measured right before the lingual nerve block. Fifteen minutes after the PNB, the pain was measured again with a VAS. Overall, both the placebo injection with saline and the PNB using lidocaine did not result in a significant decrease in the initial BMS pain. Yet, results recorded two different types of responders. The first group was called the peripheral group. Interestingly, the lingual PNB gave good results and caused the pain to decrease significantly. However, the placebo group did not have any decrease in pain. The second one, which they named the central group, reacted the opposite way. This shows that there is heterogeneity within the pathophysiology of BMS, as some are centrally driven and some peripherally driven. More research is needed on the matter before using lingual LA PNBs as a standardized treatment for certain types of BMS.

Topical LA vs PNB

Although topical LA application is not a form of injection due to its very common use with lidocaine in the treatment for BMS and the comparison to injections,⁶³ a small section on the matter has been added to this narrative review. Some studies confirm that there is a mixed reaction to topical or intramucosal use of LA in BMS. This possibly indicates a missed pathophysiology of a centralized, mixed, or peripheral neuronal drive. Furthermore, the literature suggests that the oral burning associated with BMS may be due to other peripheral pain pathways in some patients compared to others. Formaker et al studied the use of topical lidocaine to erase pain in BMS patients.⁶⁴ The results of this study on 33 patients with BMS showed that the intensity of the two chemical stimuli was statistically significantly reduced thanks to the LA. However, 12 patients had an increase in the burning sensation, and only 7 of the 33 had a decrease after the anesthetic placement.

Persistent Idiopathic Facial or Intraoral Pain *Occipital nerve block.*

Only one study of 20 patients reported successful pain management in occipital and trigeminal neuralgias using LA occipital nerve PNBs; however, there was a poor response in patients with persistent idiopathic facial pain (20%).⁴²

Discussion

Orofacial pain is mostly cared for with pharmacologic treatment and increasingly with psychologic interventions. Unfortunately, the available evidence is of low quality. Several reviews highlight the small amount

of data to justify the use of therapeutic PNBs in OFP.^{65–68} A more recent meta-analysis confirmed that the evidence for PNBs as a medical intervention in OFP has a GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) level of C.⁶⁵ The evidence for PNBs in TMDs is limited, but shows that PNBs with hyaluronate and corticosteroids may be effective for some of them. A recent narrative review³ reported similar findings. LA PNBs are not very effective for idiopathic types of chronic facial pain.⁶⁹

There is emerging evidence for the use of BTX-A in trigeminal neuralgia and for PHN. However, despite high-level evidence for BTX-A in PTNP outside the trigeminal system, there is no evidence for its use for PTNP within the trigeminal system. Despite PNBs (either LA combined with steroid or BTX-A) gaining GRADE A-level evidence for neurovascular pain conditions in the orofacial region, the evidence remains poor for their use in nonneurovascular OFP conditions. Importantly, standardized applications of neural blockades are missing. There is a need for future clinical studies of therapeutic PNBs in OFP conditions, particularly with regard to BTX-A for neuropathic pain.

There are distinct limitations in using PNBs for pain management. Possible confounders of a response to a neural block are numerous, and, with regard to the literature, there is a lack of agreed-upon diagnostic criteria, a high prevalence of the placebo effect, and many other fundamentally poorly designed study standards are overlooked. As there is a high-level evidence base for repeated LA PNBs in headaches and other pain conditions, this provides an exciting prospect for future clinical studies of therapeutic PNBs in OFP conditions. In addition, a recent study highlights the significant limitations of the existing research in this area.⁶ It reports that the pain assessments are often limited and lack a holistic approach, with no investigations into patient satisfaction or psychologic and physical functioning. Without a standardized approach in design of OFP studies, there will be significant limitations in improving care and reducing related health care cost.⁶

Importantly, sensitivity and specificity must be considered. Poor sensitivity and specificity lead to misdiagnosis and possible future problems for the patient. In chronic pain especially, phenomena like sensitization or sympathetically maintained pain, as well as refractory and referred pain, can occur, so care must be taken. Hogan et al previously stated that it is important to be critical when conducting diagnostic blocks, as the available research and evidence on how to perform PNBs are limited.^{13,70} Although it is an older study, it shows that qualitative evidence is still lacking for all PNBs in OFP. The over-

all amount of evidence and the study of Hogan et al show that there is not enough evidence to be sure of the specificity and sensitivity for PNBs and locates what will cause a false positive and false negative. It can be concluded from this that it is important to take into consideration the below information and to interpret the results of a PNB carefully. Hogan et al thoroughly described what to consider in their review, stating all the issues with false positives and false negatives, and so including sensitivity and specificity. Understanding how compromised one's assumption of the outcome of a PNB may be is crucial. The sensitivity and specificity of the intended technique are compromised due to the rarity of the OFP conditions being treated. Other limitations that must be considered include the anatomy and function of nerves. Therefore, it needs to be ensured that the LA PNB will not influence the function; more precisely, the sensory function of another branch besides the target or even another nerve.

Another consideration when using a PNB is that the pain source lays peripherally to the injection site, as the block might not work for troubleshooting in a more distal area to the painful pathology. It must be verified that the pain has gone away because the afferent signaling of that specific nerve has been blocked, as the LA works on afferent pathways. This means that the signaling from the pathology must be blocked to conclude that the site is the cause for pain. Another anatomical issue could be the type of nerve fibers. When using LA, one must be aware of what type of fibers the LA will block; ie, whether they are small or large fibers. This is called spinal processing and must be contemplated. Very importantly, referred pain is a phenomenon with substantial implications when it comes to PNBs. The presence of referred pain can cause misdiagnosis and unsuccessful treatment of a chronic pain syndrome, as well as a false belief about the source of the pain.

Two other processes that need to be investigated are central and spinal sensitization. If these processes have started, then the use of PNBs in a patient's treatment plan might not be effective and successful. In other words, the afferent signals might be stopped by the peripheral LA block, but the dorsal horns might have been sensitized, and thus they will still be giving the perception of pain to the patient. This is part of the phenomenon called neuronal plasticity. Allodynia is another example of neuronal plasticity. Due to a nerve injury or neuronal changes in chronic pain, the nerve fibers change. Low-firing neurons can become more sensitive and react to normally nonnoxious stimuli. The specialist involved will then conclude wrongly that the area is not involved, as it is not reacting to the injection clinically.

Additionally, differences in the builds of the neuronal system from individual to individual need to be considered by the practitioner when applying a PNB. There are several varieties possible both within a patient and within the population, not only in the central system, but also peripherally. For example, the possible bordering dermatome overlap is known, as is that the cranial cervical area can have from three to nine anastomoses. That is why using markers present on the surface or looked for with palpations is not reliable for finding the deviating anatomies. However, an older small cohort study of five patients reported that no adjacent neurosensory deficits were detected outside the blocked regions in the trigeminal system.⁷¹

There are restrictions with LA as well. The type of agent and whether additives are used will impact the effectiveness and duration of the block. The optimal dosage and concentration must be determined, and there must be good quality evidence for the most efficient volume of the LA agent. If the concentration of the LA is not correct, the sodium channels might not be fully blocked, meaning that pain will still be perceived by the patient. The needed amount will also depend on the activity of the nerve. The more the nerve is active, the more the sodium channels will open, and therefore the more LA can attach to the channels. Hence, the nerve will be deactivated more efficiently.

An active nerve is called being in a phasic state, and an inactive nerve will be in a tonic state. The phasic block is more powerful than a tonic block.

An LA PNB does not have a full-sensation-straight-to-no-sensation effect. After the injection, the mechanism of blocking the pain will start first. Then the mechanical stimuli will be blocked a little while after the analgesic effect. As described above, this can have an impact on the success of the PNB, because, depending on the agent, the afferent stimuli might not be fully blocked, and therefore the pain is still perceived after the PNB.

The placebo effect of LA PNBs must be contemplated as a limitation of a PNB, as it is not the PNB causing the pain to improve, but the patient's ability to alter the pain subconsciously. Hogan et al¹³ explained that when a placebo is given to relieve acute pain, the placebo effect will reduce the pain almost one-third of the time. It has been proven by Petersen et al⁷² that patients with neuropathic pain can experience a placebo effect after LA injections. Their experience showed no effect in evoked nor spontaneous pain, but, statistically, the placebo effect was highly present with regard to hyperalgesia. Similarly, there are several randomized placebo-controlled trials for different OFP disorders registering the implications of a placebo effect.

Furthermore, the doctor's involvement must be considered. Lasaosa et al have set up a consensus advising and giving guidelines to practitioners to make sure they are performing LA PNBs for orofacial chronic pain pathologies safely and effectively.⁷³ Some practical tips regarding PNBs used for headaches are provided by Patel et al.⁷⁴ Not only is knowledge of the neuronal and anatomical surroundings of the injection area important, but adequate education is needed before applying LA PNBs. Knowing anatomy and agent specifications are without a doubt crucial, especially with the arteries in proximity. Therefore, the specialist should always aspirate to avoid hematomas. Although allergies to LA agents are rare, the allergen must be recognized as an ester called para-aminobenzoic acid.⁷⁵ This will have a huge impact on the success and complications after injection. Furthermore, the specialist's attitude toward the patient will also contribute to a placebo effect. Following the narrative review of Blumenfeld et al, it can be concluded that contraindications are relative and there is a lack of evidence.⁷⁶

In addition, heterotopic pain must be considered and excluded to optimize outcome assessment; however, PNBs can be used to exclude referred pain.⁷⁷ Thus, the assumption that pain is alleviated due to specific nerve afferent signaling being blocked may be inaccurate on many levels.^{13,70}

Despite these procedural limitations, the low level of evidence in using PNBs for chronic OFP is mainly due to the lack of pRCTs. The evidence base for therapeutic PNBs for OFP is low and highlights the need for improved research in this area. This poor evidence base is mainly due to most of the evidence being case reports or case series with limited prospective studies. In addition, the diagnostic criteria varied between studies. The use of a neural block as a therapeutic tool can be beneficial; however, the possible placebo effect of an injection must be acknowledged, and this was rarely included as a potential bias in the few prospective studies. However, there is emerging evidence for the use of onabotulinum toxin (BTX-A) in TN, with a meta-analysis featuring four pRCTs, and for PHN. However, despite high-level evidence for BTX-A in PTNP outside the trigeminal system, there is no evidence for its use for PTNP within the trigeminal system.

Conclusions

This article assessed the evidence for therapeutic PNBs in chronic OFP conditions, excluding neurovascular conditions. This narrative review highlights the lack of evidence for therapeutic PNBs for non-neurovascular OFP, with the exception of TN, where 4 RCTs reported GRADE A- to B-level evidence for treating patients with refractory TN using BTX-A.

Despite PNBs (either LA combined with steroid or BTX-A PNBs) gaining GRADE A-level evidence for neurovascular pain conditions such as migraine, within the orofacial region, the evidence remains poor for their use in nonarticular TMDs, TN, PHN, PTNP, and idiopathic facial pain, including BMS. There is a need for future clinical studies of therapeutic PNBs in OFP conditions, particularly with regard to BTX-A, for neuropathic pain.

Acknowledgments

All authors have researched, co-written, and approved the paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors report no conflicts of interest.

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