Up-to Date Review And Case Report

Injection of ropivacaine combined with pregabalin in a patient with post-traumatic trigeminal neuropathic pain

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Abstract – Introduction: Post-traumatic painful trigeminal neuropathy is a chronic facial pain secondary to trigeminal nerve injury. The treatment of this pain is a therapeutic issue due to the alteration of quality of life that it generates. Observation: A 58-year-old man whose main history of facial trauma has been consulted in the Odontology Department for bilateral trigeminal neuropathic pain that has been evolving for several months. The interrogation revealed continuous pain like electric shocks in the canine areas and daily painful exacerbations. Hyperesthesia and allodynia were found on clinical examination. The patient had received several treatments, oral and local, without significant improvement. As a last resort, injections of ropivacaine every 2 weeks associated with pregabalin (200 mg/day) were performed. At 6 months, there was a clear decrease in the burning sensation and a complete disappearance of painful exacerbations. Discussion: Two studies have recently shown the benefit of the combination of an antiepileptic and a local analgesic in the treatment of classical trigeminal neuralgia, justifying their use in a context of post-traumatic neuropathic pain. Conclusion: Further studies with higher levels of evidence are needed to confirm these preliminary results.

Introduction

The French Pain Society (Société Française D’étude Et De Traitement De La Douleur) has officially defined neuropathy as a “pain associated with an injury or disease affecting the somatosensory system.” Painful post-traumatic neuropathies (PPTN) constitute 12% of all neuropathic pain [1]. The latter are defined as pain associated with nerve deafferentation mediated by peripheral nerves, generally caused by the formation of post-traumatic neuroma [2]. They combine a continuous sensation of burning or electrical shocks with intermittent exacerbations. The neurological examination may reveal hypoesthesia, hyperaesthesia or allodynia in the affected nerve area.

Level-1 analgesics such as paracetamol and aspirin are rarely effective in relieving neuropathic pain. Strong opioids can ameliorate pain, but because of associated long-term side effects, their usage should be limited to treating chronic pain [3]. Thus, as an alternative treatment, practitioners should include another class of agents in their treatment plan.

Therefore, the use of first-line oral treatments such as antidepressants, antiepileptics, and other topical treatments like capsaicin at 0.025% is recommended [4]. However, their frequent side effects sometimes preclude their usage with certain patients, and there is only a moderate, observable effect in only 30% patients [5]. Thus, other therapeutic alternatives are required.

Combination therapy with an antiepileptic and local anesthetic injections has been recently shown to result in symptomatic improvement in the management of classical trigeminal neuralgia [3,6], justifying the use of this strategy in PPTN. The case being reported here is that of a patient presenting with PPTN who received the above-described combination therapy.

Clinical observation

A 58-year-old patient was referred for treatment because she had been experiencing chronic post-traumatic neuropathic pain in the anterior maxillary area. The pain had been evolving for more than 3 months. His medical history revealed type-I, type-II, type-III LeFort fractures associated with a naso-orbito-ethmoido-frontal disjunction (NOE) following a road accident (Fig. 1). The pain began 6 months after the injury.
The patient experience with chronic bilateral symptoms resembling electric shocks and were rated 7/10 on the numeric pain rating scale (NPRS), which were accompanied by daily painful exacerbations rated 10/10 on the scale. On clinical examination, palpation of the canine teeth revealed the presence of dynamic, mechanical allodynia on the vestibular level. The patient had a score of seven out of 10 on DN4, or Douleur Neuropathique 4 (neuropathy pain) questionnaire supporting the diagnosis of neuropathic pain.

The clinical picture therefore presented all the criteria necessary to establish a diagnosis of PPTN according to the International Classification of Headache Disorders 3rd edition (ICHD-3) classification system.

Initially, the patient received 80 mg triamcinolone (Kenacort) injections to the endobuccal scar bands, but did not show any perceptible improvement. Gabapentin (GBP) treatment at 1200 mg in three doses per day was then administered for 2 months. This treatment was substituted for a 0.025% capsicum tincture because the patient had developed a sensation of numbness in the nasolabial region and the persistent pain had not decreased in frequency or intensity. The tincture was directly administered on the maxillary vestibular mucosa, 3 times per day.

After 3 months of this topical treatment, no improvement in the symptomatology was observed. Therefore, duloxetine at a dose of 60 mg once per day was initiated and was subsequently increased to 120 mg per day, but no symptomatic improvement was observed.

As a final recourse, ropivacaine (RPC) injections were administered to the scar bands; these were combined with 100 mg of pregabalin administered both in the morning and the evening. The patient received 4 ml RPC injections at 2.5 mg/ml doses approximately every 2 weeks for 6 months. At 3 months, the response to treatment was very satisfactory with a decrease in the intensity of the continuous pain sensation (NPRS 3/10) and a reduction in the quantity of exacerbation episodes to two per month. At 6 months, the continuous pains persisted (NPRS 2/10) but the painful exacerbations had completely disappeared.

Discussion

The management of neuropathic pain is complex because of the heterogeneity of its etiologies, symptoms, and pathogenic mechanisms. The primary treatment objective when managing these pains is to decrease their intensity and improve the quality of life of the affected patients. These pains are subjective symptoms described by the patient according to their characteristics and intensity. The use of validated questionnaires like DN4 or painDETECT serve as helpful tools in establishing the diagnosis of neuropathic pain despite their limited sensitivity in diagnosing PPTN [7,8]. DN4 is a diagnostic tool used in France; seven of its items are related to symptomatology (burning, painful cold sensation, electric shocks, tingling sensation, prickling sensation, numbness, and/or itching) and three items are related to the clinical examination (hypoesthesia when touched, hypoesthesia when injected, pain on rubbing).

In addition to physical pain, these patients also have an altered quality of life. This alteration is manifested by mood disorders (depression, anxiety) sleep disorders, and difficulty concentrating [6], making it a public health issue.

Neuropathic pain is difficult to treat. Antiepileptics and antidepressants are currently the first-line drugs recommended for the treating neuropathic pain.

However, various side effects (drowsiness, psychiatric disorders, headaches, dizziness, etc.), drug interactions, and the gradual increase in doses administered over a long period are causes of poor compliance with analgesic treatment [4].

The treatment of PPNT is based solely on the use of antiepileptics (GBP, carbamazepine (CBZ), pregabalin) as well as tricyclic antidepressants (amitriptyline). The response to the majority of these medications is unpredictable because it varies among patients [5]. In the case presented, there was no observable improvement under GBP and duloxetine.

Recently, two randomized studies evaluated the effectiveness of a combined therapeutic treatment where an antiepileptic was paired with a local anesthetic in the treatment of classical trigeminal neuralgia [3,6]. This combination therapy included an antiepileptic (GBP at 300–900 mg per day or CBZ at 400–1200 mg per day) together with a local anesthetic (RPC 2 ml at 2 mg/ml). The first study (CBZ + RPC vs. CBZ) showed a significant decrease in the pain...
intensity scores, the number of paroxysmal pain crises, as well as a reduction in the daily intake of medications, thereby facilitating a reduction in the side effects of the oral treatments. The second study (GBP + RPC vs. GBP vs. RPC) showed a reduction in the pain intensity and improved long-term action compared to that of the GBP monotherapy, with the added advantage of an improved patient quality of life. These results are similar to those observed in our patient who was treated for PPTN.

Other studies have shown a particular relevance of peripheral anesthetic blocks in the prevention of chronic neuropathic pain after breast cancer surgery. In one study, it was found that paravertebral anesthetic blocks could decrease the risk of developing persistent pain 6 months after surgery in 25% of the patients [9].

The development of neuropathic pain is triggered by the onset of spontaneous activity from the damaged afferent fibers and sensory neurons. Another study evaluated whether early nerve blocking would curtail this spontaneous activity and thus aid in the prevention of neuropathic pain [10]. Indeed, the transitory local administration of a nerve blocker (bupivacaine or tetracaine) for 3–7 days immediately following the injury would permanently decrease the development of painful neuropathic symptoms. However, no therapeutic effect was observed when the administration of drugs after 10 days.

It can therefore be assumed that an early administration of local anesthetics to the trigeminal nerves in our patient could have limited the onset of PPTN.

The mechanisms of pharmacodynamic action of RPC and pregabalin on post-traumatic neuropathic pain only confirm the preliminary results observed. Post-traumatic, neuropathic pain is characterized by the combination of abnormal activity discharges (within injured nerves) and metabolic modifications. These abnormal electrical activities are ectopic and are generated at the nerve endings. They are due to realignment of the ion channels acting on membrane excitability. Among these channels, there is overexpression and an accumulation of voltage-dependent sodium channels in the dorsal ganglion neurons and trigeminal neurons resulting in a lowering of the threshold of activation of the fibers as well as a positive regulation of certain subtypes of sodium channels [11].

RPC is a local anesthetic giving rise to a sensory block associated with a limited and stable motor block. The drug acts on these voltage-dependent sodium channels by reversibly decreasing the membrane permeability of nerve fibers to sodium ions. Thus, the depolarization rate decreases and the excitability threshold increases, inducing a local blockage of the nerve impulses. This mechanism of action could thus explain the relevance of this treatment to post-traumatic neuropathic pain.

In addition, following a peripheral nerve injury, there is overexpression and upregulation of the voltage-dependent α2δ calcium channel subunits of the dorsal root ganglion [12]. This contributes to an exaggeration of neuronal responses to the sensory cutaneous stimuli. Pregabalin is a structural analog of the GABA neurotransmitter that binds at the presynaptic level voltage-dependent α2δ calcium channel subunit of the nerve ganglion. Its attachment to this subunit decreases the calcium influx induced by depolarization at the nerve endings, which decreases the release of several excitatory neurotransmitters (glutamate, norepinephrine, substance P) at the synaptic level [13]. The modulation of the neurotransmitter release contributes to the inhibition of neuropathic pain induced by peripheral nerve injury.

Conclusion

The combination of an antiepileptic drug (GBP or pregabalin) and a local anesthetic (RPC) may be effective in the treatment of post-traumatic trigeminal neuropathic pain. Studies with higher levels of evidence are needed to confirm our findings.

Conflicts of interest: The authors declare that they have no conflicts of interest in relation to this article.

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