I cannabinoidi nel trattamento della nevralgia del trigemino

Case report

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Summary

Trigeminal neuralgia is the most common craniofacial pain syndrome. This disorder causes severe facial pain and is described as very acute, similar to an electric shock to the jaw, eye region, teeth or gums. The authors present a clinical case involving a 46-year-old patient with trigeminal neuralgia; in this study, cannabinoid treatment (19% THC; <1% CBD) showed good pain relief.

Riassunto

La nevralgia del trigemino è la sindrome dolorosa craniofacciale più comune. È un disturbo che provoca forti dolori al viso e viene descritto come acutissimo, simile a una scossa elettrica alla mascella, alla regione oculare, ai denti o alle gengive. Gli autori presentano un caso clinico che ha coinvolto un paziente di 46 anni affetto da nevralgia del trigemino; in questo studio, il trattamento con cannabinoidi (19% THC; <1% CBD) si è dimostrato efficace nel controllo del dolore.

Key words

Trigeminal neuralgia, cannabinoids, medical cannabis, chronic pain, analgesia

Parole chiave

Nevralgia trigeminale, cannabinoidi, cannabis medica, dolore cronico, analgesia

Introduction

The trigeminal nerve is the fifth pair of cranial nerves. It is a mixed nerve, mainly sensory, but also composed of a small contingent of motor fibers. These two components arise directly from the neuraxis as two distinct roots: the sensory root, more voluminous, lateral to the motor and

flattened anteroposteriorly, and the motor root, smaller, medial with respect to the sensory one. Gasser's ganglion represents the real origin of the somatic sensory fibers of the trigeminal nerve. It is placed in the middle cranial fossa at the apex of the temporal pyramid in a folding of the dura mater called the Meckel's cavity.

Trigeminal neuralgia is the most common craniofacial pain syndrome. It usually develops in individuals over the age of 50. The incidence is 4 /100,000 and is the most common facial pain syndrome in this age group.

Trigeminal neuralgia is a disorder that causes severe pain in the face. It is often described as sharp shooting pain or an electric shock to the jaw, teeth, or gums. Usually, it occurs suddenly, with unpredictable, painful episodes that can last from a few seconds to several minutes, up to a few hours. The affected area of the face depends on the affected branch: the first (ophthalmic), provides the sensory innervation of the ocular region; the second (maxillary) covers the homonymous area, the upper dental arch and half of the ipsilateral nose; the third (mandibular) provides for the sensitivity of the jaw, mouth and ipsilateral lower dental arch. Often it is not possible to detect a trigger even if some actions such as blinking and chewing are automatically triggered. The attacks stop as suddenly as they begin.

Precisely the onset and duration are pathognomonic of essential trigeminal neuralgia, not to be confused with other forms of craniofacial pain, for which it is easier to find an origin. It is thought that trigeminal neuralgia is often caused by the conflict between the Gasser ganglion and / or the course of the nerve and vascular malformations, tumors or other injuries including inflammatory types.[1]

Evidence suggests that in 95% of cases, neuralgia is caused by pressure on the trigeminal nerve, located near the entrance to the brainstem (the lowest part of the brain that merges with the spinal cord). It is not clear why this pressure can cause painful attacks in some people but not in others. Not all those who have a compressed trigeminal nerve, in fact, suffer from neuralgia.

It could be that, in some cases, pressure on the nerve wears down the outer protective layer (myelin sheath), causing uncontrollable pain signals that run throughout the nerve.

However, this does not clearly explain why one can experience periods without symptoms or why pain relief is immediate when, after a successful operation, the blood vessels are pulled away from the nerve.

Trigeminal neuralgia to date is one of the most complex clinical pictures of pain to be defined and treated, both from the pharmacological point of view and from the point of view of invasive or minimally invasive interventions.

In the present clinical case report, the standard antiepileptic drug therapy with carbazepine 400 mg rp, opioids and multivitamin (complex B) has not proved useful in the treatment of trigeminal neuralgia.

Cannabinoids are a class of chemical compounds that are increasingly recognized as potential therapeutic options for a range of conditions.[2] Evidence suggests that cannabinoids may prove useful in pain modulation by inhibiting neuronal transmission in pain pathways.

Case report

A 46-year-old man suffering from trigeminal neuralgia for over five years presented neuropathic pain in the right suborbital facial region, described using the Numerical Rating Scale (NRS) of 10

points. From the anamnesis, there were no obvious traumas, neither otolaryngological interventions, nor odontostomatological problems.

The patient reports unilateral pain attacks with sudden onset and lasting from a few minutes to a few hours. Several triggers have been identified such as: exposure to the sun, eating, chewing, washing the face or teeth, exposure to the wind and, in particular, shaving.

The treatment initially was carmbamazepine (dose of 400 mg rp twice a day) and tapentadol (maximum dose of 300 mg twice a day).

Regardless of etiology, the key mechanism underlying paroxysmal pain in trigeminal neuralgia is focal demyelination of primary trigeminal afferents near the trigeminal root entrance that become hyperexcitable. According to this pathophysiological mechanism, voltage-gated, frequency-gated sodium channel blockers are ideal candidates for reducing the high-frequency discharge that causes pain similar to electric shocks. Consequently, carbamazepine is a first-line drug for the long-term treatment of trigeminal neuralgia. Its action results in the stabilization of the hyperexcited neuronal membranes and the inhibition of reactivations.[3] Tapentadol is a potent centrally acting analgesic that acts as a μ-opioid receptor agonist and a norepinephrine reuptake inhibitor, in fact it is also indicated in neuropathic pain.

Furthemore, in association with pharmacological therapy, an infraorbital nerve block (both for diagnostic and therapeutic purposes) with lidocaine 1% (10mg/ml) 1 ml was performed.

Initial therapy was not effective in treating pain, due to side effects such as decreased appetite, anxiety, confusion, drowsiness, sleep disturbances and poor pain relief (NRS 8). Onthis basis, the patient underwent Cannabinoid's therapy (19% THC; <1% CBD). He started with 5 sublingual drops twice a day, up to 10 sublingual drops 3 times a day.

A pain reduction of 50% (NRS 5) was reported during the follow-up pain assessment, started fifteen days after the beginning of treatment; on this occasion, the dosage of carbamazepine (400 mg rp once a day) and tapentadol (dose of 100 mg twice a day) was reduced. After 30 days, the patient did not take any opioids, continuing carbamazepine 400 mg rp (once a day) therapy. Ninety days after the start of treatment, pain symptoms remain tolerable (NRS 3); the patient reported a feeling of discomfort and rare "electric shocks" during intense stimuli to the face (such as shaving), but both qualities of sleep and overall quality of life were improved. As side effects, the patient experienced modest drowsiness only in the first ten days, which early disappeared with the therapy adjustments. Still (120 days after the start of therapy) the patient continues the treatment with cannabinoids (19% THC; <1% CBD) 10 sublingual drops 3 times a day and carbamazepine 400 mg rp once a day with good pain relief (NRS 3).

Discussion

Among all neuralgic forms, that of the trigeminal is the most common (incidence of 4/100,000) and is limited to the distribution of one or more branches of the trigeminal nerve. It is characterized by unilateral pain attacks reported as sharp, shooting, lancinating, electric shock-like, burning, and excruciating. (4) There is a wide range of studies in the literature on the benefits of cannabinoids in trigeminal neuralgia.[5] Cannabinoid-based medicines act on the human endocannabinoid system, a network of CB1, CB2, and other receptors distributed throughout the body.[5] THC and CBD are both highly lipophilic and have poor oral bioavailability (estimated to be as low as 6%).[6] THC and CBD are both highly lipophilic and have poor oral bioavailability (estimated up to 6%).[7] Oral THC formulations exhibit variable absorption and undergo extensive hepatic first-pass metabolism resulting in lower peak plasma THC concentration relative to inhalation and a longer delay (~120

min) to reach peak concentration. Oral formulations may be useful for patients requiring symptomatic relief over a more extended period.[8]

Cannabinoids and opioids used in combination may boost the analgesic effects of opioids. Moreover, in patients suffering from chronic pain, some open-label and real-world studies have found that initiation of cannabinoid-based medicines could have implications for opioid-sparing. In case study

of Reiman and Abrams ([9,10]), 97% of patients with chronic pain reported that they could decrease their opiate dose, and 92% found the side effects more tolerable with cannabinoids than opiates.[9,10]

The prescription of cannabis for medical use in Italy is regulated by the Decree of the Ministry of Health of 9 November 2015. It can be prescribed through a therapeutic plan through the SSN (Servizio Sanitario Nazionale) and used in chronic pain when associated with multiple sclerosis, spinal cord injuries and other syndromes and only when conventional or standard therapies are ineffective.[11]

There is a theoretical risk of drug–drug interactions between some cannabinoids and some concomitant medications.[12,13] However, these have not been well studied in clinical practice, and more drug-interaction studies are urgently needed to establish the extent of any interactions, including dose-dependent effects, especially with common medications that patients may be receiving alongside cannabinoids. Caution should be exercised with any concomitant medication that is metabolized by the CYP450 complex due to pharmacokinetic interactions with THC or CBD;[14] however, the exact mechanisms of these interactions and their clinical relevance remain unknown.

Common adverse events observed in the concomitant use of Cannabinoids compound and Carbamazepine are drowsiness, dizziness, blurred vision, ataxia, headache, nausea, and rash;[15] however, in the present case report, only a transient side effect was reported by the subject, disappeared with therapy adjustments.

In a study published in 2004, the authors reported a positive role of cannabinoids in the management of trigeminal neuralgia.[1] We have observed that cannabinoid treatment had a noticeable effect. In the present case report, we obtained a reduction of the NRS values> 50% after fifteen days and an NRS value of 3 after 90 days. Treatment with cannabinoids is a safe method, causing minimal side effects.[16]

Conclusion

The present case report shows that cannabinoids therapy was effective in treating pain symptoms of trigeminal neuralgia. Based on our results, cannabinoid treatment could represent an effective therapeutic option for pain symptoms of trigeminal neuralgia. At the moment, only one other patient with trigeminal neuralgia is undergoing treatment with cannabinoids, but the data in our possession is still preliminary.

Conflict of interest

The authors certify the study was conducted without conflicts of interest.

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