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Use of Tricyclic Antidepressants in Trigeminal Neuralgia

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Abstract
Trigeminal neuralgia is one of the neuropathic pains most commonly found in the head and neck region. It presents in painful episodes in the form of electric shock lasting from seconds to two minutes, when trigger points are triggered in intra and extraoral regions. Classified as a chronic pain, trigeminal neuralgia is capable of catastrophically altering the patient's quality of life. With the review of articles in Portuguese language, articles in English language, books and journals searched in databases such as LILACS, PUBMED and SCIELO, a survey of existing data from the year 1993 to the year 2018 was carried out, and the words used to per-form this research were tricyclic antidepressants, trigeminal neuralgia, neuropathic pain and dentistry. This study aims to understand how trigeminal neuralgia occurs and to evaluate the possible treatments for it, focusing on the pharmacological treatment with tricyclic antidepressants, aiming to provide a positive result in the treatment of pain. And so we found positive results of the action of these drugs on the pathology.

Keywords: Tricyclic antidepressants; Trigeminal neuralgia; Neuropathic pain; Dentistry.

Introduction

The Neuralgia is pain felt in one or more nerves. The Trigeminal Neuralgia is caused by lesion or disease in the somatosensory nervous system, specifically on the 5th cranial nerve (trigeminal nerve). This nerve gets its name because it has three branches: the maxillary, mandible and ophthalmic nerves; carries sensory and motor information, predominantly sensory, from the face to the brain and controls the muscles involved in mastication.

Trigeminal neuralgia is the most feared of neuralgias, affects mainly females, classified as lancinating peripheral neuropathic pain, in electric shock, of sudden attack lasting from 2 seconds to 2 minutes and can occur several times a day, thus affecting the patient's quality of life. It usually occurs by the contact of a vein or artery with the nerve, generating pressure on the nerve and the appearance of hypersensitivity, mechanoallodynia, thermal hyperalgesia, hyperpathy, neurogenic

inflammation and autonomic dysregulation are observed.

Its initial and control treatment is pharmacological, with first-line drugs (Tricyclic Antidepressants and Gabapentinoids) [1].

Tricyclic antidepressants are drugs that act on the limbic system by increasing noradrenaline and serotonin in the synaptic cleft, blocking the reuptake of amines by the nerve terminals, however, they do not prominently influence the normal organism in its basal state, they only correct anomalous conditions. Antidepressants can be classified according to their chemical structure or pharmacological convenience, and TCAs (Tricyclic Antidepressants) are divided into two groups: secondary amines (protriptyline, desmethylimipramine, and nortriptyline) and tertiary amines (amitriptyline, trimipramine, doxepin, and imipramine) [2].

Although the exact mechanism of action of TCAs has not been fully explained, it is known that at the presynaptic level they block the reuptake of monoamines, such as norepinephrine with secondary amines, serotonin with tertiary amines, and, to a lesser extent, dopamine. TCAs block cholinergic, histaminergic, serotonergic and, more rarely, dopaminergic receptors.

They acutely promote an increase in the efficiency of monoaminergic (and possibly GABAergic) transmission, involving the noradrenergic and serotonergic systems, increasing the synaptic concentration of norepinephrine and serotonin by blocking reuptake. The anti-neuralgic action of TCAs is not essentially linked to the improvement of depression, analgesia can be measured by changes in the central concentration of monoamines, individually serotonin, in addition to the direct and indirect effect of TCAs on endogenous opioid systems [2] .

The dental surgeon may be the first professional consulted by a patient with TN (Trigeminal Neuralgia). It is of fundamental importance that these professionals are able to establish a correct diagnosis [3].

Systemic pharmacotherapy is the most common approach to the treatment of neuropathic pain. Antidepressants, anticonvulsants have moderate efficacy and often the increase in dose is limited by adverse effects. A therapeutic screening, monotherapy or combined, should seek the most appropriate treatment for each case. Continuous reassessment should focus both on pain control and on improving the patient's quality of life [4].

Methodology

The methodology used was a literature review whose objective is to investigate a certain topic so that the researcher can confront, confirm or refute its proposition. With the review of articles in Portuguese, articles in English, Spanish, books and journals searched in databases such as LILACS, PUBMED AND SCIELO, a survey of existing data from 1983 to 2019 was carried out, and the words used to carry out this search were tricyclic antidepressants, trigeminal neuralgia, neuropathic pain, and dentistry.

Results (Review)

The present study investigated the relationship between antidepressants and Trigeminal Neuralgia (TN).

Trigeminal Neuralgia is one of the facial diseases with the most painful symptomatology [5,6,7,8,9].

Trigeminal neuralgia is a unilateral disorder characterized by electrical shock-like neuropathic pain near the distribution of the trigeminal nerve with sudden onset and termination. Being a syndrome characterized by paroxysmal facial pain. The main etiologic hypothesis of essential trigeminal neuralgia is vascular compression over the sensory root. NT is classified as classic or primary or idiopathic and symptomatic or secondary [5,9,10,11,12,13].

The causes of trigeminal neuralgia are usually detectable by their clinical presentation, such as tumors; inflammatory changes and others [13, 14, 15].

In primary care in the UK, between 2002 and 2005, the incidences (per 100,000 person-years of observation) were 27 (95% confidence interval (CI) 26 to 29) for trigeminal neuralgia [16]. However, the incidence of trigeminal neuralgia has also been estimated to be 4 per 100,000 per year [17,18] and 3.9 per 100,000 [19].

The prevalence of TN was estimated at 107.5 men and 200.2 women per 1 million inhabitants. The incidence rate of TN was 4.3 per 100,000 in the US population, with the age-adjusted rate for women being significantly higher than for men [20].

Thus, specific guidelines have been developed for the pharmacological management of neuropathic pain such as trigeminal neuralgia, with recommendations for medications from a variety of therapeutic classes, including anticonvulsants, antidepressants, and opioid analgesics [SULTAN 2008, MOORE 2012, LUNN 2014, 21,22 ,23].

For the treatment of neuropathic pain, the Brazilian Medical Association (AMB) and the International Association for the Study of Pain (IASP) recommend the use of antidepressants.

tricyclics (amitriptyline, nortriptyline, imipramine and clomipramine) [23].

The main mechanism of antidepressants that inhibit neuropathic pain is, first, to increase noradrenaline in the spinal cord and, second, to act on the locus coeruleus, directly inhibiting pain and activating the compromised descending noradrenergic inhibitory system.

Dopamine and 5-HT also have an increase in the central nervous system and may potentiate the inhibitory effects of noradrenaline in an auxiliary manner [22,24].

Imipramine is a tricyclic antidepressant that has analgesic efficacy in NP and rheumatic pain. Its analgesic action is independent of the antidepressant action [4,22,23,25].

Amitriptyline is considered the main antidepressant analgesic, this does not mean that other antidepressants, tricyclic and non-tricyclic, are less effective, but that most of the clinical evidence available is in relation to amitriptyline [4,23,26].

Regarding dosage, amitriptyline should be administered with an initial dose of 10 mg, with a gradual increase every 3-7 days, up to a maximum dose of 150 mg in a single dose at night, preferably [4,23].

Nortriptyline is a tricyclic antidepressant and the main active metabolite of amitriptyline. Most commonly used to treat neuropathic pain worldwide, regardless of licensed indications. It is recommended in European, British and US guidelines, although not always as a first-line treatment [ATTAL 2010; NICE 2013, 23.27].

Nortriptyline is sometimes preferred over amitriptyline because it reportedly has a lower incidence of associated adverse effects, may increase patient compliance, and may be particularly helpful in older adults who are more likely to experience adverse effects such as confusion and agitation and postural hypotension [8,23].

Nortriptyline is available in 10 mg and 25 mg tablets and as an oral solution. When used to treat neuropathic pain, an initial dose of 10 mg per day can be gradually increased to 75 mg per day. This is usually given as a single dose overnight to reduce any daytime effects [8,23].

The mechanism of action of nortriptyline in the treatment of neuropathic pain remains unclear, although it is known to inhibit the reuptake of serotonin and noradrenaline. It is likely that the mechanism is different from that of depression, as analgesia with

antidepressants are often obtained at lower doses than the onset of any antidepressant effect; adverse events associated with its use usually disappear after two or three weeks [8,23].

In addition to the TCAs, six systematic reviews investigated treatments for trigeminal neuralgia. Conclusive evidence on the efficacy of trigeminal neuralgia was presented for rTMS57 and carbamazepine. Lamotrigine and pimozide were evaluated positively for refractory trigeminal neuralgia. Other systematic reviews were inconclusive (carbamazepine versus topiramate, tizanidine, pimozide, and acupuncture; 0.5% proparacaine hydrochloride versus placebo) or unclear statements in their conclusions (neurosurgical interventions: peripheral interventions, cutaneous interventions applied to the procedure and two modalities of stereotaxic radiosurgery) [28].

Conclusion

The present study showed an association between trigeminal neuralgia and tricyclic antidepressants. Thus, TCAs emerge as an effective alternative for the relief of trigeminal neuralgia.

These findings indicate the possibility of drug interventions with TCAs to break this pain cycle in order to reduce the sequelae during the occurrence of trigeminal neuralgia.

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