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Review on Trigeminal Neuralgia

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Abstract:

Aim: To write a review on trigeminal neuralgia.

Objective: To analyze the competence of the new trends over the old trends and decipher the advantages and disadvantages of both.

Background: Trigeminal Neuralgia is a clinical syndrome characterized by brief, repetitive, extremely intense paroxysms of unilateral facial pain. The pain can be triggered by cutaneous stimuli including those resulting from daily activities like brushing the teeth, chewing or talking. The condition may begin at any age, although it tends to occur more frequently with advancing age and it affects women somewhat more often than men. Medical therapy is considered the primary treatment for patients with trigeminal neuralgia. Sometimes, surgical therapy is also offered if medical therapy is inefficient or causes too many side effects.

Method: Reviews on trigeminal neuralgia were collected from journals with a PubMED , Science Direct and Scopus Index.

Results: The articles collected were based on the various treatments and diagnostics of pain of trigeminal neuralgia.

Keywords: Antiepileptic drugs, neuropathic pain, nociceptive impulses, trigeminal neuralgia, tic douloureux, visual analog scale,

INTRODUCTION:

According to the definition provided by the International Association for the Study of Pain, pain is defined as "an unpleasant and negative sensory and emotional experience associated with actual or potential tissue damage".[1] The character of pain depends on its location, type of dysfunction of the particular region, and stage of the disease.

Trigeminal neuralgia (TN) is a unilateral disorder characterized by brief electric shock-like pains, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve. [2] The disorder is most common in patients aged 50-70 years and is more common in women.[3,4] It is the most widely recognized neuropathic pain of the face and has been shown to be profoundly distressing the patient's well-being [5]. Neuralgia is a symptom of nerve dysfunction present within the brain stem or within the nerve segment running to the trigeminal ganglion located within the base of the middle cranial fossa.

Main etiological factors responsible for neuralgia include vasculoneural conflict consisting of compression the trigeminal nerve near the dorsal root entry zone [6-10] by an overlaying blood vessel [6] at the site of neural connection to the brain stem, within the region of the superior cerebellar artery, the basilar artery, the vertebral artery, or the petrosal vein. Neuralgia may be the result of head injury or inflammation of nerve within its myelin sheath. The disorder may also be associated with other diseases such as multiple sclerosis or tumors that compress the nerve and disturb its function.[11,12-21,22] .

MATERIALS AND METHODS:

Researches on Trigeminal neuralgia were collected from the Journals with a PubMed Index. Articles collected were based on the treatment and diagnostics of pain of trigeminal neuralgia.

DISCUSSION:

Anatomy:

The trigeminal nerve is the fifth cranial pair (CN V). It is a sensory and motor nerve, consisting of a large sensory root and small motor root. The sensory root transmits sensory information from the unilateral hemiside and is divided into three branches which correspond to three different skin areas (dermatomes): V1, V2 and V3. The motor root innervates the unilateral masticator muscles. This root cannot be distinguished from the sensory root in MRI. It has a common extracranial pathway with the common trunk of the nerve and root of CN V3 over the whole pathway.[23] The gasserian ganglion is located in the trigeminal fossa (Meckel cave) of the petrous bone in the middle cranial fossa. It contains the first-order general somatic sensory fibers that carry pain, temperature, and touch. The peripheral processes of neurons in the ganglion form the 3 divisions of the trigeminal nerve (i.e., ophthalmic, maxillary, and mandibular). The ophthalmic division exits the cranium via the superior orbital fissure; the maxillary and mandibular divisions exit via the foramen rotundum and foramen ovale, respectively.

The majority of nociceptive impulses from the orofacial region are mainly mediated by the trigeminal nerve. The action potentials are transmitted from its peripheral branches, ophthalmic (V1), maxillary (V2), and mandibular (V3), by pseudo-unipolar neurons with the cell bodies located in the trigeminal (gasserian or semilunar) ganglion. From the trigeminal ganglion, the central processes of these cells follow the trigeminal sensory root and enter the lateral portion of the pons in a region frequently referred to as the trigeminal root entry zone (REZ). [24]

Causes:

Trigeminal neuralgia can be caused by a lesion of the sensory nuclei of CN V or the sensory root and its branches up to the skin. The spinal nucleus of CN V in which pain

fibres relay has broad distribution over the brainstem and the upper cervical spine. This explains why cervical medullar, bulbar, pons and mesencephalic lesions can be responsible for CN V neuralgia.[24] Most cases are caused by compression of the trigeminal nerve root within a few millimeters of entry into the pons.[25,26]. The nerve impingement is often accompanied by a demyelination of sensory fibers within the nerve root or the root entry zone, or less commonly in the brainstem.[27] In a small fraction of patients, the cause of TN cannot be identified. [28]

Diagnosis:

The diagnosis of TN is usually based on the characteristic clinical picture. The key feature is a sudden and severe lancinating pain, usually unilateral, precipitated by lightly touching facial zones. This pain occurs in paroxysms, within the trigeminal nerve distribution; typically involving the maxillary nerve (V2) or mandibular nerve (V3) distribution.[25] Pain symptoms may be categorized under the following:[29]

- Dysaesthesia (abnormal perception of pain)
- Allodynia (due to a stimulus which does not normally provoke pain)
- Hyperalgesia (an increased sensitivity to pain)

In some patients, these painful bursts can be triggered simply by cutaneous contact with a trigger zone or during movement. Where this trigger zone exists, there is a refractory period at the end of an episode of pain during which the subject can touch the trigger zone without this causing pain. Neurological examination of these patients is usually normal. Pain is alleviated by inhibitors of the sodium channels. Neurovascular compression is the principal cause of trigeminal neuralgia.[23]

Standard of Pain:

Pain attacks start abruptly and last several seconds but may persist for 1 to 2 minutes. [30,31] After each episode, there is usually a refractive period during which stimulation of the trigger zone will not induce pain.[32] The frequency of attacks depends on the sensitivity and location of the trigger area. This pain occurs in paroxysms, within the trigeminal nerve distribution; typically involving the maxillary nerve (V2) or mandibular nerve (V3) distribution and lasts for a fraction of a second to 2 minutes.[25]

Current trigeminal neuralgia pain scales:

Visual Analog Scale

The prototypical assessment of pain intensity is the Visual Analog Scale (VAS)[33]. This instrument consists of a 10 cm (100 mm) line with verbal anchors at each end (e.g.- 0 representing "no pain" and 100 representing "worst pain"). Patients mark on this line the point which they feel best represents their perception of pain (Fig.I, Fig.II). It is a continuous scale that allows the estimation of pain intensity. This can also be used as a verbal rating scale asking patients to express their pain as range from 0 to 10. VAS scoring has linear scoring properties (i.e. the difference in pain between each successive increment equals to 10) [33]. Thus, a VAS pain score of 60 mm indicates twice as much pain as a VAS score of 30 mm.

Composite Scales

Composite scales in the neurological literature of trigeminal neuralgia have also been used.[34] These include 2 elements. The first part often involves a measure of pain intensity in 3 to 5 categories specifying the level of pain (e.g. none, some and severe). Another method used in some studies is the "global assessment in change", which is expressed as a percentage decrease in pain. [35] The second part of these composite scales describes the level of medication usage such as no medication use, reduced medication use and continued medication use.

McGill Pain Questionnaire

The McGill Pain Questionnaire (MPQ) which allows the patient to indicate easily the quality of his/her pain using such descriptors as throbbing, shooting, distressing, excruciating etc. It contains a total of 78 words which can assess sensory and affective pain qualities. The patient is asked to circle a word that best describes his pain in each word set. The rank value for each descriptor is based on its position in the word set [e.g. – flickering(1), quivering(2), pulsing(3), throbbing(4), beating(5), pounding(6), jumping(1), flashing(2), shooting(3) etc.] The sum of the rank values is the Pain Rating Index (PRI). Minimum PRI is 0 and maximum PRI is 78. PRI can be compared at subsequent visits of the patient and is also used for comparison within two or more patients. [36]

Types of Neuralgia:

Trigeminal neuropathic pain (TNP) disorders, as typical, atypical, and post-herpetic trigeminal neuralgias, are commonly incapacitating conditions with pain that is either spontaneous or can be evoked by harmless but crucial activities, such as eating and talking, or by light touch.[37]

Typical-TN is described as a disorder with an incidence of 3 to 5 cases *per* 100,000 persons, affecting, on average, elderly people. The pain is characterized as sharp and shooting. Severe brief paroxysmal pain is spontaneous or elicited when the trigger-point, usually located in the oral or peri-oral region, is stimulated by light touch. It is postulated that typical-TN is caused by compression of the trigeminal root by a blood vessel or tumors at the level of the root entry zone (REZ).to the facial skin. [37]

Interestingly most trigeminal neuralgia patients experience a toothache-like pain with continuous, aching, or burning quality resembling atypical-TN pain. TN presents most commonly in the lower two branches of the trigeminal nerve. Very often it presents intraorally with triggers around the teeth [38] and hence many patients will undergo irreversible dental treatment unnecessarily. [39]

Atypical-TN affects a larger number of patients and is described in a wider variety of pain descriptors, including burning and throbbing. Nonetheless, patients have also reported, to a lesser degree, sharp pain as typical-TN. [40] For those patients, the mild to severe pain is usually constant, with a characteristic after-sensation.

It should be mentioned that neuralgia may be of either spontaneous (primary) or symptomatic (secondary) form. Both forms differ significantly in the character and intensity of pain. In spontaneous neuralgia, the acute, paroxysmal, and piercing pain occurs at a single facial

location to spread along the course of the nerve on one side, sometimes a dozen or so times a day, without forewarning periods. Pain episodes may last several seconds to several minutes. [17-19] Primary neuralgia is often accompanied by facial muscle contractures, increased salivation, running nose, and skin redness. Stimuli that most commonly cause the pain are trivial and everyday causes such as wind gusts, sudden changes in air temperature, bright light, sharp sounds, or delicate touch (e.g., shaving in males). [17-19]

In contrast to the spontaneous neuralgia, its symptomatic (secondary) form is associated with pain that increases gradually, has different nature, and persists with no interruptions. The pain becomes intensified in heat. It may be a result of numerous local or generalized causes such as odontitis, cysts, sharp socket edges, tumors within the mouth, and the maxillo-ethmoidal massif, disorders of the maxillary sinuses or the middle ear. [17,19]

Treatment:

Medical Treatment:

Many medical and surgical treatments are available. Most patients respond well to pharmacotherapy; carbamazepine and oxcarbazepine are antiepileptic drugs and are used as first line therapy, while lamotrigine and baclofen are considered second therapy. Other drugs such as botulinum toxin-A are alternative treatments. Botulinum toxin type A (BTX-A), one of the seven antigenically different botulinum neurotoxins derived from *Clostridium botulinum*, appears to be the most potent subtype.[41]

According to current evidence-based treatment guidelines published in 2008 from the American Academy of Neurology (AAN), and the European Federation of Neurological Societies (EFNS),[42] carbamazepine is established as effective (level A) and oxcarbazepine is probably effective (level B) for controlling pain in classic TN. These guidelines recommend carbamazepine (200-1200 mg/d) and oxcarbazepine (600-1800 mg/d) as a first-line therapy for classic TN.

Carbamazepine acts by inhibiting voltage-gated sodium channels, thereby reducing the excitability of neural membranes. Carbamazepine has also been shown to potentiate gamma aminobutyric acid (GABA) receptors made up of alpha1, beta2, and gamma2 subunits. This may be relevant to its efficacy in neuropathic pain.[43] Common side effects include sedation, dizziness, nausea, vomiting, diplopia, memory problems, ataxia, elevation of hepatic enzymes, and hyponatremia, which may contraindicate it for elderly patients.

Oxcarbazepine is a keto-analogue of carbamazepine that is rapidly converted into its pharmacologically active 10-monohydroxy metabolite. Oxcarbazepine is an acceptable alternative to carbamazepine, which may have provided pain relief but has caused unacceptable adverse effects. Better tolerability can also be considered an advantage over carbamazepine.[44]

According to Dalessio, medications work by interrupting the temporal summation of afferent impulses that precipitate the attack.[45]Anticonvulsant medications pose risks of sedation and ataxia, particularly in elderly patients, which may make driving or operating machinery hazardous. They also may pose risks to the liver and the hematologic system. Thus, documentation of patient education about these potential risks is important.

Surgical Treatment:

Surgical options are available if medications are no longer effective or tolerated. Microvascular decompression, gamma knife radiosurgery, and percutaneous rhizotomies are most promising surgical alternatives. In the case of a failure of medical treatment, two main techniques that are suggested are thermocoagulation of Gasser's ganglion and neurovascular decompression.

Prior to considering surgery, all trigeminal neuralgia patients should have a MRI, with close attention being paid to the posterior fossa. Imaging is performed to rule out other causes of compression of the trigeminal nerve such as mass lesions, large vessels, or other vascular malformations.[46]

Gamma Knife radiosurgery, also called stereotactic radiosurgery, is a very precise form of therapeutic radiology. It uses beams of highly-focused gamma rays to treat small to medium size lesions, usually in the brain. Many beams of gamma radiation join to focus on the lesion under treatment, providing a very intense dose of radiation without a surgical incision or opening.[47] Neurosurgeons all over the world prefer Gamma Knife radiosurgery, either instead of or in addition to traditional brain surgery and radiation therapy. It's known for its precision and high success rate. Gamma Knife radiosurgery kills or shrinks brain tumors or stops their growth nearly 90 percent of the time. The pain recurrence rate is low for patients who initially attain complete relief. Trigeminal neuralgia patients who experience recurrent pain during the long-term follow-up despite initial pain relief after radiosurgery can be treated with second radiosurgery procedure.[46]

Themoregulation of Gasser"s ganglion is the treatment of essential Trigeminal Neuralgia with controlled increments of radiofrequency heating from an electrode inserted in the Gasserian ganglion or the posterior rootlets. Assuming that the less myelinated small fibers (A delta and C) are more sensitive to the heat than the heavily myelinated A beta and A alpha fibers, gradually controlled thermo coagulation could produce a differential destruction of pain fibers. Patients are known to experience immediate relief from this treatment.[48]

Microvascular decompression (MVD) is a surgical procedure to relieve the symptoms (pain, muscle twitching) caused by compression of a nerve by an artery or vein. MVD involves surgically opening the skull (craniotomy) and exposing the nerve at the base of the brainstem to insert a tiny sponge between the compressing vessel and the nerve. This sponge isolates the nerve from the pulsating effect and pressure of the blood vessel.[49] Mortality rate for MVD ranges from 0.2% to 0.5%. There is a 4% incidence of postoperative morbidity such as cerebro-spinal fluid (CSF) leak, infarct, or hematoma formation.[50]

Disadvantages of Surgical Procedure:

No surgery is without risks. General complications of any surgery include bleeding, infection, blood clots, and reactions to anesthesia. Specific complications related to a craniotomy may include stroke, seizures, venous sinus

occlusion, swelling of the brain, and CSF leak. The most common complication related to MVD is nerve damage, which varies depending on the nerve being treated; these include hearing loss, double vision, facial numbness or paralysis, hoarseness, difficulty swallowing (dysphagia), and unsteady gait. [49]

CONCLUSION:

The treatment measures for trigeminal neuralgia were summed up. Antiepileptic drugs like carbamazepine and oxcarbazepine are used as first line therapy. Surgical options are available if medications are no longer effective or tolerated. Microvascular decompression, gamma knife radiosurgery, and percutaneous rhizotomies are most promising surgical alternatives. Pain scales such as the Visual Analog Scale and the McGill Pain Questionnaire are used to identify the levels of pain.

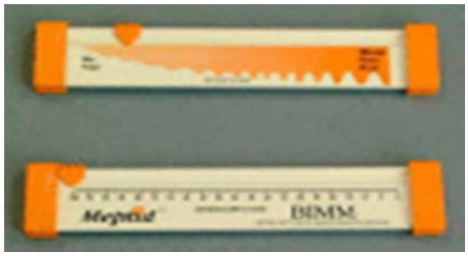

Fig.I Visual Analog Scale

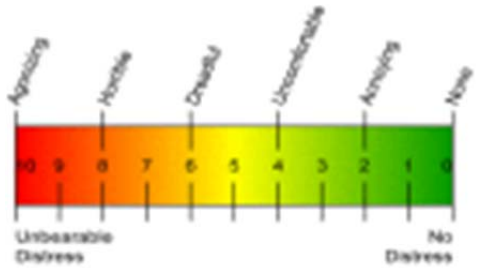

Fig. II Visual Analog Scale

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