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Review Article

MANAGEMENT OF TRIGEMINAL NEURALGIA: A REVIEW ON PERIPHERAL SURGICAL INTERVENTIONS

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Abstract

Trigeminal Neuralgia or tic douloureux is a disease affecting older patients, and thus office based "minimally invasive" therapy is inherently attractive. The condition is characterized by paroxysmal pain so excruciating and sudden, like a shock, which lasts a few seconds to two minutes. The treatment of trigeminal neuralgia over the last three centuries has included an assortment of ineffective and bizarre interventions such as hemlock, arsenic, tooth extractions, purging, bleeding, carotid ligation, abdominal steam, and others. In the present era, treatment modalities of trigeminal neuralgia are broadly categorized into medical management, peripheral surgical procedures and central surgical procedures. The aim of this article is to review the literature on the use of peripheral surgical interventions for management of this condition.

Keywords: Pathology, Peripheral Surgical Interventions, Review, Trigeminal Neuralgia, Alcohol.

Introduction

Trigeminal Neuralgia (TN) is the most widely recognized neuropathic pain of the face and has been shown to be profoundly distressing to the patient's wellbeing.[1]The International Association for the Study of Pain defines TN as "sudden, usually unilateral, severe, brief stabbing or lancinating, recurrent episodes of pain in one or more branches of the trigeminal nerve".[2] The condition affects the middle or older individuals aged 50-70 years and mostly women.[3,4] The etiology is still a mystery but compression of the trigeminal nerve near the dorsal root entry zone is a major causative or contributory factor.[5-9] In a small fraction of patients, the cause of TN cannot be identified.[10]

The treatment of TN has intrigued the minds and taxed the ingenuity of oral surgeons and physicians for a long time. An ideal treatment is one that causes no morbidity and preserves the normal sensation of the face. Such a sensation preserving, absolutely safe and permanently successful treatment does not exist as yet.[11] Current management

of this condition is divided into medical and surgical with medication in the form of anticonvulsants (Carbamazepine) been the first line of treatment. Surgical options are considered when medical treatment fails due to either poor or diminishing response to drugs or due to their unacceptable side effects.[12]

Surgical interventions are best classified according to the principal target: peripheral techniques targeting portions of the trigeminal nerve distal to the Gasserion ganglion; percutaneous Gasserion ganglion techniques targeting the ganglion itself; gamma knife radiosurgery targeting the trigeminal root and posterior fossa decompression techniques.[13]Neurosurgeons recommend radical techniques like microvascular decompression or radiofrequency thermocoagulation. These procedures require general anesthesia and carry significant morbidity and even mortality risks. With radiofrequency thermocoagulation, the reported complications have included anesthesia dolorosa (0-13%), motor paresis, (0-53%) and miscellaneous eye problems (0-13%).[14]Although microvascular decompression is definitively the treatment of choice for TN with the lowest rates of pain recurrence, it is also the most invasive procedure with highest rate of serious complications.[15] Therefore it is reserved largely for younger patients with acceptable surgical and anesthetic risks.

Many elderly patients are infirm and unable to travel long distances for specialized treatment or are unable to cope with the side effects of these invasive procedures. Therefore there remains a need for relatively simple, minimally invasive methods of pain control that can be carried out on an outpatient basis and that may be repeated without additional risks. Peripheral surgical techniques of pain control fulfill these criteria.

Peripheral Surgical Procedures

Peripheral surgical options for TN include neurectomy, peripheral injections of different chemical agents and cryotherapy. These procedures broadly interfere with the afferent pathways from the trigger zones to prevent stimulation of afferent conduction pathways.[16, 17]Generally, they are easy to perform and well tolerated with relatively few serious side effects. On the other hand, they have a limited duration of action and patients must be advised that they may require repeated procedures. In patients considered unsuitable for neurosurgical owing to comorbidities or age, and in those unable to tolerate medical treatment, these procedures may become their sole form of management and repeatability becomes another important issue in such patients.[18]

Relatively few contraindications exist to most peripheral techniques, because they can generally be performed under local anesthesia. However, medical considerations include immunosuppression and congenital or acquired bleeding diathesis, particularly if considering neurectomy or cryotherapy, because they require a surgical flap to be raised. The presence of local infection surrounding the nerve would also be a relative contraindication to peripheral treatment.

1: Neurectomy

It is one of the simplest peripheral surgical procedures that includes the sectioning and avulsion of the terminal branch of the trigeminal nerve. The regrowth of terminal fibres is prevented by subsequent obliteration of the canal. Surgical access to the second and third divisions is via the intra-oral route avoiding postoperative facial scars. Some authors use a transfacial access to the second division due to lower chances of infection of the postoperative wound and reduced postoperative oedema.[19, 20]

The pain free period after one neurectomy is varied in the literature: 24-32 months by

Quinn J.H.[21] (1965), 26.5 months by Freemont A.J. and Millac P.[22] (1985), 12.2 months by Bagatin M. and Arko V.[23] (1984), at least 2 years by Hong-Sai L.[24] (1999) and 16.3 months by Cerovic R.[25] (2009). It is also observed that with repeated neurectomies on the same neural branch, the time of remission decreases.[25-27]Some authors state that the response of the patients to carbamazepine in case of recurrence improves after neurectomy[28, 29] and lower doses of the medication are needed.[25, 29]

Although the procedure is one of the simplest of the peripheral surgical procedures, it is not without disadvantages. Complete anesthesia in the nerve distribution is inevitable sequelae of the procedure. Recurrence of pain is to be expected and although retreatment is a feasible option, it is technically more challenging due to presence of scar tissue making the raising of the surgical flap and identification of the nerve progressively more difficult. Such a procedure eliminates the further role for peripheral techniques because of removal of the terminal branches and this is one reason why its use has been largely abandoned.[27, 30]

2: Peripheral Injections

A number of chemical agents are used to provide immediate symptom relief. However, the effect is only temporary and the duration of relief depends on the agent used.

A: alcohol:

Alcohol injections have been suggested in the management of TN since the early 20th century but its role remains controversial.[31]Although they are reasonably effective in producing short to medium term pain relief, the procedure does carry risks and is only temporary.

Two distinct techniques are described for peripheral injection of alcohol and these have been well described by Stookey and Ransohoff.[31] In one of the techniques, a transcutaneous injection of the nerve at the skull base at the foramen ovale or foramen rotundum is performed whilst in the other technique; the injection is more distal as the nerve passes recognizable landmarks in the facial skeleton. Both techniques involve the injection of the relevant nerve with local anesthetic followed by injection of 0.5-1.0 ml absolute alcohol once analgesia is confirmed. The techniques mandate accurate placement of injections as alcohol is highly toxic and use of aspiration technique to avoid injecting into the accompanying vessels.[32-34]

The median duration of pain relief ranges from 6 months to more than 24 months with some variation in the results obtained from the different peripheral branches: first division injections lasting less than second division, which last less than third division.[17]

Advantages include rapidity of the procedure, reliability with most authors reporting high rates of pain relief and high patient satisfaction with most patients reporting that they would undergo further injections when the pain returns.[35] There is no evidence to show that age or number of previous procedures affects the time to relapse for alcohol injections or that the use of such injections while awaiting other treatments is detrimental to their outcome. Disadvantages include transient burning sensation on injection and reduced effectiveness with repeated administration due to the dense fibrotic tissue around the nerve region reducing penetration of the fluids[33] although a recent study found no reduction in the effectiveness even when as many as 14 blocks were administered in one individual over many years.[17]

Although a widely used agent, its use is not without complications. Reported complications include sudden loss of vision, local oedema, local tissue necrosis, muscle palsy, sensory disturbances, neuropathic

pain and severe trismus if mandibular muscle is involved.[16, 29, 33, 36] Alternatives to alcohol injections include glycerol injections, cryotherapy or neurectomy.

B: Glycerol

Hakanson first injected anhydrous glycerol into the trigeminal cistern in 1981.[37] Since then glycerol has been reported to be effective in the treatment of TN.[37-40] Stajcic in 1989introduced the peripheral injection technique and established that the procedure gave comparable results to percutaneous retrogasserion glycerol injections with faster onset of pain and with minimal complications.[38]

Although the exact mechanism of pain relief produced by glycerol in TN is still unknown, several hypotheses have been suggested. Stajcic (1989) and Lunsford (1985) reported structural changes in the nerve fibres after glycerol injection.[41, 42]Rengachary et al (1983) reported myelin disintegration and axonolysis with glycerol injection in the peripheral nerves.[43] Al-Khateeb T.L. (1998) hypothesized that the pain relief obtained with glycerol injection is related to partial dehydration and compression of the affected nerve with little evidence of actual destruction.[39]

The median duration of pain relief is 9 months according to Wilkinson.[44] Fardy et al compared peripheral alcohol injections to glycerol injections and found the former to have a longer duration of pain relief with no greater morbidity.[45]

The success rates of glycerol injections are comparable to alcohol injections but technically it is more difficult to administer due to its viscosity although it is not as painful as absolute alcohol and repeated injections can be administered. Glycerol injections have limitations due to anatomical variations in the course of the nerve. Also at higher temperatures, glycerol becomes less viscous and may disperse from the site at the time of injection.[46] Complications are minor and include hypoesthesia or dysesthesia that resolve within months, transient hematoma, ecchymosis and temporary mandibular hypomobility.[11]

C: Streptomycin/Lidocaine

It has been reported that topical application of streptomycin can achieve pain relief in different types of facial pain such as odontalgia [Halasz I. (1965)] [47] and cluster-tic syndrome [Kreiner M. (1996)]. [48] However, with regards to its favorable effects in TN, reports are controversial. Sokolovic et al (1986) in their preliminary study on 20 patients claimed good results with peripheral injections of streptomycin/lidocaine.[49]The patients were given 5 injections at 1 week intervals. All patients obtained pain relief, without any sensory loss, only 4 patients had a recurrence. The remaining 16 patients remained pain free upto a period of 30 months. Stajcic et al (1990) in a double-blind controlled trial showed that these injections were only initially effective.[50]On a contrary, Bittar and Graff-Radeford (1993) concluded that streptomycin/lidocaine injections were ineffective in the treatment of both idiopathic TN and post-traumatic neural pain.[51]

The mechanism of pain relief is not completely understood but it is believed that this drug produces a repolarization of depolarized nerve due to a membrane stabilizing effect[52] and also affects the release of acetylcholine at the nerve endings.[52, 53]After infiltration of streptomycin the conduction velocity of the nerve is reduced.[54-56]

Streptomycin produces axonal damage peripherally in the nerve bundles covering approximately one-fifth of the entire circumference.[50]This suggests that there is little probability of affecting those axons that transmit trigger stimuli with a single injection of streptomycin. This coincides with the pure clinical observation that

streptomycin should be given in 5 weekly peripheral injections as mentioned by Sokolovic et al[49] and Stajcic et al[50]. The extent of morphological changes affecting fibres responsible for the trigger mechanism of peripheral nerve treated with streptomycin is unpredictable regardless of the number of injections. Therefore, the result of peripheral streptomycin/ lignocaine injections in the treatment of neuralgic pain can also vary, ranging from positive effects to unfavourable results. Due to insufficient research data there is a need for high quality randomized controlled trials in this area of medicine.

Possible advantages include cost effectiveness, ease of availability, repeated administrations possible without fear of fibrosis as compared to alcohol injections. It is also well tolerated and lowers the doses of anti-convulsants and therefore the side effects of these drugs. The sensory function of the nerve is unaffected as streptomycin is a potentially selective neuroablative. The side effects are minimal and pain associated with the deposition of the solution is reduced by the effect of lidocaine.

Streptomycin, an antibiotic which has been attempted in the past to relieve orofacial pain, has tremendous scope for further research in the future.

D: Local Anesthetics

Injections of local anesthetics can be helpful in the diagnosis of TN as well as confirming the trigger zones. Peripheral nerve block using high concentrations of local anesthetics prolongs the analgesic effect in patients with TN[18, 57].

Clinical and experimental data indicate that changes in the expression of voltage-gated sodium channels play a key role in the pathogenesis of neuropathic pain and that drugs that block these channels are potentially therapeutic in TN[58]. In addition, recent data show that local anesthetics may have pain-relieving actions at targets other than sodium channels; these targets include neuronal G protein-coupled receptors and binding sites on immune cells[58, 59].

Patients with painful peripheral neuropathy sometimes receive weeks of relief following a single local anesthetic block of the painful region[60]. One postulated mechanism for the long term effect of local anesthetics on the trigeminal nerve is Wallerian degeneration. Histologically, the extra fascicular administration of local anesthetics at clinical concentrations can alter perineural permeability, causing endoneurial oedema, increased endoneurial fluid pressure, andWallerian degeneration with Schwann cell injury and axonal dystrophy which may reduce allodynia, hyperalgesia, and trigger point hypersensitivity[63].

The mean duration of pain relief with local anesthetic injections is of short duration as compared to alcohol injections. In a few case reports on the clinical application of high concentration local anaesthetics for the treatment of TN, pain relief lasted for 2.2 weeks to 14 months.[18, 57, 60]Goto et al used an infraorbital nerve block with 4% tetracaine dissolved in 0.5% bupivacaine to treat older TN patients who did not wish to have a neurolytic block or surgical treatment, and reported that the analgesic effects continued for more than 3 months.[57]

Sato et al reported two cases of idiopathic superior laryngeal neuralgia treated with a superior laryngeal nerve block using a high concentration of lidocaine; the pain was alleviated for 1 year without the need to continue block therapy after 10 treatments using 1 mL of 10% lidocaine over 12 days.[61]They postulated that the effective period in previous cases was shorter because the injected local anaesthetic remained in the trigger zone for a shorter time. In a recent study by Dergin G. et al, the authors used a pain pump and an epidural catheter and administered 0.25% bupivacaine hydrochloride via continuous administration

in 14 patients with TN.[16]They observed pain relief in 11 of 14 patients for upto 9 months without jeopardising the sensory function.

TN block using high concentration local anaesthetics is reversible and non-traumatic, and is appropriate for further surgical interventions like microvascular decompression.[62] In addition; it allows patients to continue their daily social activities without antiepileptic drugs, which cause a lack of concentration, drowsiness and dizziness. It reduces allodynia, hyperalgesia and trigger point hypersensitivity without sensorial loss. Reported complications are minimal compared to alcohol injections.[16]

E: Botulinum Toxin Type A

Botulinum toxin (BTX) is a naturally occurring neurotoxin that is produced by gram positive anaerobic bacteria Clostridium botulinum. There are seven distinct antigenic subtypes of BTX of which BTX type A (BTX-A) appears to be the most potent subtype.[63]BTX- A is reported to be effective in the treatment of migraine and occipital neuralgia.[64] Literature supports the effectiveness of submucosal or subcutaneous injections of BTX-A for adult TN patients.[65]

The actual mechanism of pain relief is not well understood. Some authors believe that injection of BTX inhibits secretion of acetylcholine in nerve endings, causing relaxation of muscles and finally relief of pain, whereas others think that the injection stops secretion of some nociceptive neuropeptides in addition to acetylcholine, which may help to prevent pain sensation.[66-68]

Regarding the duration of pain relief, two studies suggest that the effect of a single BTX-An injection could last for 6 months or approximately 24 weeks [69, 70]whereas a few studies show the efficacy reduced at 4-8 weeks after treatment.[65]

The most important question concerning BTX-A is the dosage in management of TN. The most commonly used dose of BTX-A is 20-75 U. However, Piovesanet al[71] found that 6-9 U of BTX-A induced significant decreases in the pain area and intensity, suggesting that lower doses are also feasible. Türket al[70] also reported the effectiveness after treatment with 100 U of BTX-A. Because no study was designed to compare the therapeutic efficacy of BTX-A at different doses, the optimal dose cannot be concluded.

BTX-A is well tolerated by the patients with minimal injections, has a faster onset of action with its significant effect reaching within 1-2 weeks and maximum effect within 4-6 weeks and has limited systemic adverse events.[65] Although BTX-A was well tolerated in TN patients, transient facial asymmetry, transient oedema, eyelid ptosis, dysesthesia and difficulty in chewing were still reported in 6 studies.[65]

BTX-A represents a promising treatment of TN with favorable risk-to-benefit ratio. However, well designed randomized, controlled, double-blinded trials are still lacking. Future adequately powered studies are needed to investigate the optimal dose of BTX-A treatment, the duration of therapeutic efficacy and the time and indications for repeat injection.

3: Cryotherapy

Cryotherapy to eliminate pain in peripheral nerves was described by Lloyd et al in 1976.[72] Good results were achieved with open nitrogen spray, the so-called spray freezing of the infra-orbital nerve.[73] However the technique required exposure of the nerve and damage of the adjacent tissue was likely if the spray was inaccurately applied. To counteract these disadvantages, a penetrating freezing technique with transmucosal application of the cryoprobe was developed.[74]

The 'penetrating freezing' technique has the following advantages: surgical exposure of the nerve as required with the spray-freezing

or contact freezing methods is no longer necessary; lesions in the oral cavity resulting from liquid nitrogen dripping or running off are prevented[75]; the short duration of intervention and the intervention itself result in little mental stress to the patient; the small wound produced by inserting the probe transmucosally heals quickly and involves only a small risk of infection; the probe is easy to handle and the design is technically simple; and the treatment can be repeated as often as necessary.

Although cryotherapy reliably eliminates attacks of pain, recurrences are observed as early as 6-8 months after treatment[76-78] which is early as compared to other surgical methods. Therapeutic efficacy might be improved by placing the cryoprobe more accurately by using intra-operative radiography.[77] Lower temperatures at the tip of the cryoprobe and greater freezing capacity also lengthen the pain free interval.

An important advantage compared to other surgical methods is the restoration of sensation within 3-4 months.[77, 78] Destruction of the nerve sheath, considered to be one of the causes of complications such as painful neuromas that may be seen after radical operations does not occur with cryotherapy. In addition the procedure can be repeated when pain recurs.

Post-operative complications include local infections and atypical pains.

Conclusion

The management of TN remains controversial with, to date, no ideal treatment. Any treatment of TN is successful as long as it eliminates the pain. Peripheral surgical procedures offer short to medium term relief of symptoms and may be offered to allow pain relief while neurosurgical procedures are being considered. However, they should not be considered as an alternative to neurosurgical procedures like microvascular decompression, which has definite long lasting results with relatively few post-operative complications compared to other surgical methods. There are very few studies to support the use of one peripheral surgical technique over another, and the choice is likely to depend on local experience and availability.

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