

The Evolution of Peripheral Nerve Treatment for Trigeminal Neuralgia - Peripheral Nerve Surgery

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ABSTRAK

Neuralgia trigeminal biasanya menyebabkan kesakitan yang teruk dan tiba-tiba pada bahagian muka. Walaupun suntikan saraf periferi dapat mengurangkan kesakitan dalam rawatan neuralgia trigeminal, kesan ini tidak berkekalan. Rawatan pembedahan pula merupakan rawatan alternatif bagi pesakit di mana rawatan perubatan tidak berkesan atau pesakit mengalami kesan sampingan yang teruk akibat ubat anti-konvulsan. Kebanyakan petugas kesihatan yang muda mungkin tidak sedar bahawa rawatan pembedahan adalah rawatan utama neuralgia trigeminal dari awal abad ke-19 sehingga tahun 1960-an. Ulasan ini merencanakan evolusi rawatan saraf periferi bagi neuralgia trigeminal sepanjang 150 tahun yang lalu.

Kata kunci: krioterapi, laser, neuralgia trigeminal, neurektomi periferi

ABSTRACT

Trigeminal neuralgia typically presents with a sudden and severe facial pain. Although peripheral nerve injection can produce good pain relief in the treatment of trigeminal neuralgia, their effect may not be permanent. Surgical treatment has always been an alternative for patients who do not respond well to medical treatment or, for those who are severely affected by the side effects of anti-convulsants. Unknown to most young healthcare providers, surgical treatment was the first line treatment at the turn of the 19th century till 1960s. This review narrates the evolution of peripheral nerve treatment for trigeminal neuralgia over the last 150 years.

Keywords: cryotherapy, laser, peripheral neurectomy, trigeminal neuralgia

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INTRODUCTION

Trigeminal neuralgia (TN) is characterised by “recurrent unilateral brief electric shock-like pains, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve and triggered by innocuous stimuli. It may develop without apparent cause or be a result of another diagnosed disorder” (Headache Classification Committee of the International Headache Society 2013). The intensity of this paroxysmal attacks has often been reported to greatly reduce the quality of life for its sufferers (Melek et al. 2018; Zakrzewska et al. 2018). In the second part of this series, this manuscript reviews surgical options for recalcitrant TN cases when multidrug and peripheral injection approaches fail to provide pain-relief for (Ngeow et al. 2021).

PERIPHERAL NEURECTOMY

The peripheral nerve surgery, which includes neurectomy, cryotherapy and laser ablation aims to block the afferent pathway to the central nervous system. At the early part of the 19th century, different types of operations had been attempted on the peripheral branches (usually the infra- and supraorbital nerves, or the mental nerve) of the trigeminal nerve, namely neurotomy, neurectomy, evulsion and nerve stretching (Meirowsky & Pipito 1943). Neurotomy, namely the simple cutting of the nerve, was performed by Galen as early as 180 A.D. however, this procedure was shown to be ineffective on the face. Other unsuccessful

surgical technique included evulsion of the nerve by Thiersch (1889) and stretching the nerve by Vogt (1877) (Meirowsky & Pipito 1943).

Following this, peripheral neurectomy gained prominence. Peripheral neurectomy or peripheral nerve avulsion aimed at sectioning or removal of post-ganglionic peripheral trigeminal nerve. Neurectomy was first recommended by Abernethy in 1793 to prevent recurrences of the neuralgia, with modification such as crushing and cauterising the nerve was made by Von Klein (1822) or splitting the central portion longitudinally and looping it back, as suggested by Malgaigne (1843). Most important was to section the nerve proximal to its foramen, as first described by Warren in 1828 (Meirowsky & Pipito 1943). Peripheral neurectomy to terminal branches of trigeminal nerve is a straight-forward, low-risk and repeatable surgery when performed correctly (Sung 1951; Hong-Sai 1999).

Peripheral neurectomy is the oldest, most reputedly performed minimal invasive surgery by Marechal, surgeon to King Louis XIV (Fowler 1886). The first person credited to have carried out the authentic peripheral neurectomy remained controversial. Quinn (1965) has reported that Nicholas André performed this surgery in 1732, while Sung claimed that Schlichting did so in 1748 (Sung 1951). Schlichting however, had met with very little success in his attempt to divide the infraorbital nerve for facial neuralgia. With the introduction of general anaesthesia Patruban in 1853, had passed a tenotome along the floor of

orbit to section the maxillary nerve behind the orbit (Harris 1951). One surgical technique introduced to avulse the inferior alveolar nerve for the control of TN on the lower jaw/face was to trephine the mandible at the mid-zygoma level (either before or after the molar teeth removal) and the upper border of the inferior alveolar canal (Robson 1893).

Following refinement and improved experience, peripheral neurectomy (with or without gasserian root dissection) was broadly reported in both dental and surgical literatures in the late 19th century (Harris 1951; Fowler 1886; Gross 1868; Terrillon 1877). In 1886, Fowler published the first comprehensive review on the outcome of peripheral neurectomy in 83 cases which was one of the three available treatment options for TN apart from alcohol injection and ganglion root resection (this procedure was pioneered by Rose in 1892) (Harris 1951; Rose 1892; Sharpe 1918). Fowler credited a German neurosurgeon A. Wagner for popularising peripheral neurectomy (Fowler 1886). The results of peripheral nerve avulsion closed to the ganglion by Wagner's and Fowler's techniques varied; however, several subjects were found to achieve remission between 1 to 3 years and some even for life. In contrary, oral surgeons performed the peripheral neurectomy nearer to the distal end exit of nerve (Gross 1868). Following that, reports on peripheral neurectomy were scarce in between the two World Wars (Bourgoyne 1944).

After World War II (WWII), similar studies were published between 36-54

years ago (Baurmash & Mandel 1967; Ransohoff 1969; Mason 1972; Khanna & Galinde 1985). The subsequent publications of this surgical procedure were random (Freemont & Millac 1981; Murali & Rovit 1996; Cerovic 2009). Cherrick in 1972 had published a case report of peripheral neurectomy performed on a bilateral TN that was very successful with minimal postoperative complications (Cherrick 1972). The method of peripheral neurectomy for the mandibular branch of the trigeminal nerve has changed post WWII, with Ginwala's approach being introduced (Ginwala 1961). After the provision of a local anaesthetic agent, the nerve concerned was exposed and two suture loops were tied at the proximal and distal exposed portion of this nerve. Sectioning was done between these 2 knots. This was followed by grasping the distal end of the nerve at its exit at the mental foramen with a haemostat, followed by a complete avulsion. The foramen was then packed with shaved bone (Ginwala 1961). The electrocauterisation of residual proximal nerve stump after completion of nerve avulsion had been reported by Grantham and Segerberg (1952) to achieve variable outcomes, ranging from no improvement to 8-year of pain-free period. In the past, relief was reported to last over a year (Ginwala 1961). Currently, the majority of patients achieved post-surgical pain relief varying from 24 months for infraorbital and supraorbital neurectomies to 26 months for mental nerve neurectomy (Quinn 1965; Hong-Sai 1999; Mason 1972, Khanna & Galinde 1985). Nevertheless,

additional low-dose medical treatment may still be required in up to 31% of patient post-peripheral neurectomy in order to achieve complete pain relief (Khanna & Galinde 1985; Freemont & Millac 1981). However, in the past, this was not the case as medical therapy itself was not effective. Often, the patients underwent numerous peripheral neurectomy, sometimes in combination with alcohol injections.

Recurrence of neuralgia following peripheral neurectomy has frequently been reported in both past and current literatures (Cerovic 2009; Yuvaraj et al. 2019). Yadav et al. (2015) reported recurrence of TN within 6 months after surgery in 25% of their Indian patients. Recurrent TN following peripheral neurectomy can be as high as 78% with a mean follow up period of 7 years and one-half of them suffered the neuralgia within a month (Oturai et al. 1996). Recurrent TN could occur at the same nerve branch or even progress to adjacent branch(es). Many authors described a number of repeated peripheral neurectomies on trigeminal nerve divisions (Sung 1951; Murali & Rovit 1996; Cerovic 2009). Sung believed that this procedure was suitable for newly emerging cases, with intracranial surgery indicated once pain progress to other nerve branches (Sung 1951). Cerovic disagreed with repetition of peripheral neurectomy on the same nerve for more than three times as the remission time reduced after each surgery (Cerovic 2009).

In a single peripheral nerve, the recurrence of pain is associated with spontaneous nerve regeneration following peripheral neurectomy. This

issue was well-known since the early research on neurectomy (Sung 1951; Ngeow 2015) and has been confirmed in animal study (Cogan 1968). Spontaneous nerve regeneration can result in resurgence of pain after surgery as early as 3-6 months (Bagheri et al. 2004; Murali & Rovit 1996), although Quinn & Weil (1975) had found that the nerve foramina reducing in size after each time being filled with natural bone during second and third neurectomy. This hindered the proximal segment of a severed nerve from re-joining its distal end, and rendered their patients pain free status.

However, in patent foramina, the success rate of axonal regeneration depends on the severity of injury and surgical method of neurectomy. The result of axonal regeneration post-peripheral neurectomy is unpredictable as there is disruption of the connective tissue framework which is an important factor in guided regeneration (Quinn 1965). However, Sung reported peripheral nerve regeneration at 24-26 months after neurectomy in TN cases (Sung 1951). The peripheral nerves have been observed to regenerate into fine branches on subsequent surgery by Quinn (1965) and this observation has been reconfirmed in a recent case report (Ngeow 2015). Large, myelinated axon carries the triggering stimulus signal while the ascending nociceptive pathway is involved in the activation of small-diameter A-delta fibres and unmyelinated C-fibres (Law & Lilly 1995). It is known that the small-diameter myelinated (A) and unmyelinated (C) nerve fibres

recover sooner than the larger-diameter axons (A) (Fridrich 1995). This might be the reason for sensory recovery (mostly pain) being faster in TN patients compared to the unpredictable outcomes in those who have undergone surgical nerve repair (Sung 1951; Robinson et al. 2000). In conclusion, the overall failure rate of peripheral neurectomy ranges from 36% to 74% at the first and fourth year after the surgery (Mason 1972).

In view of the fact that natural bone does not normally obliterate foramina, various alternative materials have been used to prevent the regeneration of peripheral nerve such as gold foil, adipose tissue, bone wax, silver plugs, plexiglass, sterile wooden points, rubber, silastic plugs, silicone rubber, metal crews and amalgam to obliterate the bony foramina or nerve canal at the neurectomy site (Cherrick 1972; Sung 1951; Hong-Sai 1999; Ginwala 1961; Baumash & Mandel 1967; Freemont & Millac 1981; Cogan 1968). Bone wax was reported as the preferred material used in obliteration of foramina by several authors (Cherrick 1972; Murali & Rovit 1996; Chandan et al. 2014). Yet, Quinn and Weil disagreed to plug the foramina with bone or amalgam because they thought the foramina would eventually be filled up by natural bone (Quinn 1965). Having said so, no other authors had reported observing natural bone growth to occur and obliterated the foramen. Cogan had shown the effectiveness of foraminal obliteration in preventing peripheral nerve regeneration in an animal study (Cogan 1968). This method was also confirmed to reduce the failure rate of

peripheral neurectomy (Mason 1972).

More than a century ago, Beckmann was the first person to obliterate the foramen at neurectomy site using a screw and his patient enjoyed longer remission period than others (Beckman 1916). However, this practice was not practised by other authors until 1999, when Hong-Sai inserted titanium screws to obliterate foramina. Biocompatible titanium screw was found to be useful and easy to use in the obliteration of various maxillofacial foramen, and the duration of pain-free could extend up to 4 years and beyond (Hong-Sai 1999). The remission period of TN was found to be greatly increased in a prospective study by Ali et al. (2012) who placed stainless steel screws into nerve foramina. Nevertheless, the small sample size in their study with only 24 months of follow-up duration required longer duration of monitoring for the consistency of such outcome. Ngeow recently reported that pain free period can last up to 10 years following peripheral neurectomy and screw obliteration, when coupled with medical therapy (Ngeow 2015).

However, following the favourable outcomes of medical therapy and the subsequent high successful rate of complex surgical procedures included microvascular decompression and percutaneous stereotactic radiofrequency rhizotomy with less complications, peripheral neurectomy with or without obliteration has become less popular. Nevertheless, Murali and Rovit had reported an excellent result of pain relief for 5 years or more in their TN patients who were treated with peripheral neurectomy

after recurrence of pain following radiofrequency thermocoagulation (Murali & Rovi 1996). The resurgence of this surgical technique was reported by many oral surgeons in the Indian subcontinent for the past 15 years as it is used for the patients who were living in remote areas with no modern neurosurgical facilities (Bagheri et al. 2004; Chandan et al. 2014; Ali et al. 2012; Agrawal & Kambalimath 2011). The advocates of peripheral neurectomy believe that there is still a role for this surgery among those who are reluctant to go for major complicated surgery, elderly and medically compromised (Freemont & Millac 1981; Murali & Rovit 1996; Cerovic 2009).

Nevertheless, a recent critical review stated that peripheral neurectomy should not be recommended as the first-line treatment in classic TN because of a more favourable long-term outcomes could be achieved with medical therapy or central neurosurgical procedures (Yuvaraj et al. 2019). The authors found that peripheral neurectomy was associated with lesser quality and shorter duration of pain relief when compared to central neurosurgical procedure.

CRYOTHERAPY

In 1976, the use of cryotherapy by Lloyd in patients with TN had showed encouraging results (Lloyd et al. 1976). It was shown, in animal model that cryolesion produced by extreme cold had caused Wallerian degeneration of large and small fibres distal to the lesion, leading to total functional

block and, therefore, pain relief. The effect of cryogenic blockage is, however, reversible with regeneration of nerve fibres after 42 days, hence re-establishing sensory function clinically. Freezing would have to be severe to achieve such desirable results and open-nerve freezing method of cryotherapy involves surgically exposing and freezing of a peripheral branch of trigeminal nerve by direct contact of a cryoprobe with a tip temperature ranging from -50°C to -70°C under intravenous sedation or general anaesthesia. The exposed nerve is frozen for a standard 3 cycles of 2 minutes freeze and 5 minutes thaw (Poon 2000). A less invasive approach is to use radiological control and a nerve stimulator on a cryoprobe to determine the location for cryoblockade (Juniper 1991).

Animal study showed that cryotherapy to peripheral nerve had resulted in a type II Sunderland's classification of nerve injury (Whittaker 1974). More specifically, the application of extreme low temperature would ensure pan-necrosis of small pain fibres in order to avoid intensifying the pain by reducing large fibre activity but "opening the gate" with viable small pain fibres in the gate theory of Melzack and Wall (Nally 1984; Barnard 1980).

In Lloyd's study, all 6 patients with facial neuralgia treated this way were found to be pain free for a period continuing up to 112 days with a median of 21 days (Lloyd et al. 1976). Similar pain-free periods were also achieved in Bernard's group of patients afflicted with intractable facial

pain of various aetiological factors. Studies have shown that cryoanalgesia produced superior outcomes (longer pain relief period up to a maximum of 2 years 2 months) with short duration of sensory loss, absence of post-operative pain) than other methods which included sectioning of the nerve following cryoanalgesia and injection of neurolytic agents for neuralgic pain of non-herpetic origin (Poon 2000; Nally 1984; Barnard et al. 1978; Goss 1984). Several studies reported of their patients having normal sensation returned within 3 months of cryotherapy (Poon 2000; Juniper 1991).

In comparison to neurectomy, sign and symptom recur soon after cryotherapy because of its limited application to the branches of the nerve rather than the nerve division. The median time to pain recurrence reported for the infraorbital, mental and long buccal nerves is 14 months, 9 months and 11 months, respectively (Zakrzewska 1987; Zakrzewska 1991). In general, the median time to recurrence of pain is modest for cryotherapy in comparison to radiofrequency thermocoagulation (24 months) and microvascular decompression (5 years). However, when carried out repeatedly, cryotherapy was shown to provide longer pain free intervals for mental and long buccal branches as compared to the infraorbital branch (Zakrzewska 1991; Pradel et al. 2002). Hence, despite the relative ease of the procedure and the minimal, reversible post-operative risks/complications with an improvement in quality of life (Zakrzewska 1991; Zakrzewska &

Thomas 1993), some researchers do not advocate the use of cryotherapy in the management of TN (Nurmikko & Eldridge 2011). Nonetheless, it was suggested that cryotherapy should still be included as a treatment option for TN patients so that they can make a more informed choice of treatment (Zakrzewska 1991).

LASER

Light amplification by stimulated emission of radiation or commonly called laser has gained popularity in the medical field recently for its usage to cut, ablate, burn or destroy tissue. Lasers at different wavelength are also being used to stimulate tissue healing, enhance β -endorphin production, inflammation and pain attenuation. Studies have demonstrated that heat can disturb peripheral nerve excitability, hence causing conduction block (Frigyesi et al. 1975). Letcher and Goldring (1968) found that thermal injury caused selective conduction block at small delta and C-fibres while preserving the alpha and beta nerve fibres. The experimental thermal injury to nerve by Xu and Pollock (1994) has agreed that the unmyelinated C-fibres has preferential susceptibility to heat injury, which showed reversible conduction block at lower temperature and axonal degeneration at higher temperature. Therefore, heat generated by laser energy can be used as an alternative treatment modality for reducing neuropathic pain in trigeminal neuralgia.

Based on these knowledges, Sessirisombat (2017) hypothesised

that heat produced from laser can be used to reduce neuralgia. He reported favourable outcome of ablating the affected peripheral nerves with CO₂ laser in 36 patients. To perform this ablation, their affected nerves were exposed approximately 1 cm in length from their respective foramina, and were using a power of 5 W, in continuous and defocused mode on the entire exposed nerves for approximately 30 seconds. All his patients reported reduced pain up to one year post neural ablation. Ninety-four percent of his patients reported prolonged paraesthesia, with the remaining 6% having normal sensation with the neuralgia pain alleviated (Sessirisombat 2017).

Instead of ablating nerves, Deenadayalan et al. (2012) used a diode solid active semiconductor laser with aluminium gallium and arsenide as medium and a wavelength of 800-980nm to resect a peripheral nerve. The affected infraorbital nerve was exposed intraorally and resected using 2 W of power (Deenadayalan et al. 2012). They followed on by lasing for 5 seconds the residual nerve tissue within the bony canal. They completed the procedure by lasing the canal using non-continuous mode with the power of 1.5 W for 5 second.

Different studies have evaluated the effect of laser therapy in comparison with placebo irradiation or medicinal and surgical treatment. Low level laser therapy (LLLT) uses a monochromatic light source to modify the cellular and tissue function. It was first introduced about 3 decades ago with many studies done either in-vitro or in-vivo

to prove its effectiveness (Kovács et al. 1974). Even though the exact mode of action for LLLT is not fully elucidated, it is believed to increase the Adenosine Triphosphate (ATP) production and Adenosine Diphosphate (ADP)/ATP carrier activities which enhance the DNA/RNA/protein synthesis by mitochondria (Passarella 1989). Low level laser therapy has been shown to be effective in many conditions such as temporomandibular joint disorder, myofascial pain, musculoskeletal pain, and post-herpetic neuralgia hence the extension of its application to treat TN (Cotler et al. 2015; Falaki et al. 2014; Moore et al. 1989). Lasers of different wavelengths have been tested using different power setting in various studies.

Simunovic believes that He-Ne laser is the most proper laser for TN while radiation at trigger points is more effective than at any other points (Simunovic 1996). In one study, patients received 1 mW 632.5 nm 20 Hz of He-Ne laser for 20 seconds to the surrounding sites, with 30-90 seconds irradiation of the skin overlying the painful facial areas following a predetermined protocol. Control subjects received placebo sham treatment. This procedure was repeated 3 times a week, continuously for 10 weeks, with patients in the LLLT group experiencing a remarkable pain reduction in term of visual analogue score and frequency of painful episodes (Walker et al. 1988).

Gallium aluminium arsenides (GaAlAs) diode-laser (808 nm/200mW) has also been reported to provide relief from TN. Vernon and Hasbun (2008)

reported the successful outcome on two patients who became pain-free at the 12th of 20 sessions following a protocol of 6 J/pm daily irradiation with two days interval after each 5 day. In another study in Denmark, 16 patients suffering from TN were radiated with laser for 5 weeks (832 nm/30 mW) and compared with 14 patients as control group. The outcome after one year of follow up was encouraging (Eckerdal & Bastian 1996). Similarly, Pinheiro et al. (1997) found that 73.6% of their patient with TN had improved with some even became asymptomatic after being treated with diode lasers with average dose that ranged from 0.2 (632.8 nm) to 3.9 (830 nm) J/cm². Two type of wavelengths were used with the average doses of 1.8 (830 + 632.8 nm) and 5.4 J/cm² (830 + 670 nm) in an attempt to improve the absorption and penetration of the laser energy at different level of tissue. They found that visible light of 632.8 and 670 had a better effect on surface lesions while 830 nm in deeper ones (Pinheiro et al. 1997; Pinheiro et al. 1998).

One study added CO₂ laser into the array of LLLT. Kim et al. (2003) compared the effect of LLLT (He-Ne, GaAlAs and CO₂ laser) alone versus

another group patients with TN treated with laser and medication. The laser therapy alone effected more pain relief when compared with patients on the combined therapy. In contrast, a recent study on the use of LLLT in conjunction with medical therapy found that the application of LLLT for 9 sessions (3 days a week) resulted in lower severity of pain at the end of treatment in comparison to sham control group on medical therapy alone (Ebrahimi et al. 2018).

In summary, LLLT is non-invasive and well tolerated by the majority of patients who are not responsive to conventional medical treatment or who refuse to undergo invasive surgery. The treatment regime (exposure time, frequency, and duration), application techniques and device specification (wavelength and power density) vary widely depending on the availability of the facility and the experience of the surgeons. Thus, more researches are needed to identify the efficacy of the different laser energy for inclusion as the recommended treatment option of TN (Falaki et al. 2014).

CONCLUSION

Table 1: Types of surgical treatment for peripheral nerve and their effect on trigeminal neuralgia

Surgery	Types	Effect
Neurectomy		Pain relief between 1 – 3 years
Cryotherapy		Pain relief up to 2 years
Laser ablation	CO ₂ laser, 5 W, 30 seconds Diode solid active semiconductor laser, 2W, 5 seconds Low level laser He-Ne laser, 1 mW, 632.5 nm, 20 seconds GaAlAs diode laser, 200 mW, 808 nm	Pain relief up to 1 year

In conclusion, recalcitrant TN may require more invasive procedure like peripheral neurectomy, even though the procedure has been found to be not as effective as it was thought to be. As such, it should not be recommended as the first option in the treatment of TN, and methods like peripheral injections described in Part I of this article would suffice when medical therapy fails. Cryotherapy on the other hand has been shown to have increased efficacy with repeated applications. The use of laser in the treatment of trigeminal neuralgia has been reported to be effective as it is able to cut, ablate and burn the affected peripheral nerves. Low level laser therapy on the other hand, has been shown to reduce pain intensity and intake of carbamazepine. Laser of different types, wavelength and frequency require further study to elucidate the best specifications that can be used in the treatment of trigeminal neuralgia.

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