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OBLITERATING FORAMINA FOLLOWING PERIPHERAL NEURECTOMIES CAN PROLONG REMISSION OF NEURALGIA UP TO 10 YEARS

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Wei Cheong Ngeow*

*Department of Oro-Maxillofacial Surgical and Medical Sciences
Faculty of Dentistry, University of Malaya
Kuala Lumpur, Malaysia

BDS (Mal), FFDRCS (Ire), FDSRCS (Eng)
MDSc (Mal), PhD (Sheffield), FAMM

Abstract

Peripheral neurectomy is a post-ganglionic surgical procedure that involves the alvusion of a peripheral branch of the trigeminal nerve after it exits the cranium. It has been described as a simple, low-risk, repeatable surgery that can be applied to the terminal branches of the trigeminal nerve for the control of trigeminal neuralgia. However, one problem that arises is nerve regeneration, and hence the recurrence of neuralgia. The use of a titanium screw to block peripheral nerves from regenerating through various maxillofacial foramina has been described. However, the longest period of pain relief has been reported to be up to 4 years only. This article provides a historical overview of peripheral neurectomy, while at the same time describing the possibility of achieving pain relief for up to 10 years by blocking the regeneration of nerves through the insertion of a titanium screw into their respective foramina.

Keywords: trigeminal neuralgia, neurectomy, titanium screw, peripheral nerve regeneration

Introduction

Trigeminal neuralgia is defined as "sudden severe brief stabbing recurrent pains in the distribution of one or more branches of the fifth cranial nerve".[1] One of its characteristics is a severely painful condition that afflicts the elderly, particularly females and the diagnosis can usually be made solely based on the clinical signs and symptoms.Medical management is the mainstay treatment for trigeminal neuralgia, consisting in the prescription of anti-convulsants such as carbamazepine, dilantin sodium, baclofen, lamotrignine and oxcarbazepine. Diphenylhydantoin sodium (dilantin) was the first anti-convulsant reported as an effective medical therapy in 1942[2], followed by the introduction of carbamazepine two decades later.[3] They act as sodium channel stabilizers and relieve pain in trigeminal neuralgia by suppressing membrane resonance and firing in abnormal afferents. Carbamazepine is the most studied and currently remains the drug of choice for treating trigeminal neuralgia.[4] It has been reported as an effective long-term treatment in 75% of the patients for whom the drug was initially effective.[5] Carbamazepine should be changed to oxcarbazepine in the event of poor efficacy and when unacceptable side effects emerge. With patients suffering from persistent neuralgia even when the therapeutic blood levels of carbamazepine have been achieved, the second-line approach is to add another anti-convulsant such as baclofen, gabapentin, pregablin, lamotrigine, clonazepam, sodium valproate, phenytoin sodium, or even opiates.[4] Surgical treatments may be an alternative for patients who do not respond well to medical treatment or are severely affected by their side effects.[6, 7] It was reported that 44% of patients ended up in this category[5]. There are essentially two targets for surgical approaches: the peripheral nerve branch and the trigeminal ganglion. Peripheral procedures include neurolytic alcohol injection, peripheral neurectomy, radiofrequency thermocoagulation of the peripheral branches, and cryotherapy. Surgery of the trigeminal ganglion includes rhizotomy, radiofrequency thermocoagulation, decompression of ganglion or main nerve trunk and sterostatic gamma knife radiosurgery. [7, 8] Peripheral neurectomy is

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*** Corresponding author:**
Professor Dr. W.C. Ngeow,
Department of Oro-Maxillofacial Surgical and Medical Sciences Surgery,
Faculty of Dentistry,University of Malaya,
50603 Kuala Lumpur,Malaysia.
Tel: 603-79674862
Fax: 603-79674534
E-mail: ngeowy@um.edu.my

a post-ganglionic surgical procedure that involves the alvusion of a peripheral branch of the trigeminal nerve after its exit from the cranium. It has been described as a simple, low-risk, repeatable surgery that can be applied to the terminal branches of the trigeminal nerve.[9, 10] It is an ancient procedure, apparently was performed by Marechal, surgeon to Louis XIV in the fifteenth century.[11] There were conflicting reports on the first person credited to have performed authenticated peripheral neurectomy. One report has it that Nicholas André performed it in 1732[12], while another claimed Schlichting performed this procedure in 1748.[9] This procedure was extensively reported in the late 19th century in both surgical and dental literatures[11, 13] Among neurosurgeons, Fowler credited A. Wagner of Germany for popularising this procedure.[11] Fowler himself documented the outcome of peripheral neurectomy of 83 cases in his 1886 publication.[11] The peripheral nerves were avulsed as closed to the ganglion as possible by these neurosurgeons. Wagner's and Fowler's results were variable, but some of the subjects were reported to achieve remission between 1 and 3 years, while in several, for life. The oral surgeons instead removed the nerve nearer to its exit at the distal end.[13] Thereafter, there was a paucity of reports on peripheral neurectomies between the two World Wars.[14] Khanna and Galinde reported a success rate of 75%.[15] Most patients achieved pain relief that ranges from 24 months for infraorbital and supraorbital neurectomies to 26 months for mental neurectomy.[10, 13, 15-17] However, up to 31% of these patients may still require additional medicinal support to relieve symptoms after peripheral neurectomy, but usually at a lower dosage.[7, 18]

One of the problems that may arise following peripheral neurectomy is spontaneous peripheral nerve regeneration. This problem has been reported ever since the early publications on neurectomy[9] and has been confirmed in animal studies.[19] This process may subsequently result in the re-emergence of trigeminal neuralgia as early as 3-6 months post surgery.[7, 15] The extent to which axons succeed in regenerating is dependent on several factors, among which the severity of the injury and the method of neurectomy.

So, axonal regeneration in neurotmesis (as resulting from peripheral neurectomy) is less predictable because of the disruption of the connective tissue sheaths that is important to guide regeneration.[12] Nevertheless, in patients with trigeminal neuralgia, it has been reported that peripheral nerves regenerated 24-26 months after transection.[9] It is unclear why the sensation more commonly returns (usually manifesting as pain) in patients with trigeminal neuralgia as opposed to those who have undergone surgical repair for nerve damage, where the outcome is often unpredictable (9, 20). As a result, an overall failure rate of 36% and 74% has been reported at the end of the first and fourth years post-neurectomy.[17]

Therefore, various attempts have been made to block peripheral nerve regeneration in such cases, using materials such as gold foil, silver plugs, bone, fat, bone wax, plexiglass, rubber, sterile wood points, silastic plugs, silicone rubber, steel screws and amalgam to obliterate the canal or foramen where nerves were alvused.[9, 10, 18, 19, 21-23] Bone wax was among the more popular material used as reported by several authors.[23-25]

Hong-Sai found that titanium screws were useful to obliterate various maxillofacial foramina as they are biocompatible and were technically easy to use[10] Obliteration of the foramen has been shown to prevent nerve regeneration in an animal study [19] and was confirmed to be useful in reducing the failure rate after peripheral neurectomy[17] Hong-Sai reported cases of pain relief that lasted least 4 years, namely the 4 cases where titanium screw insertion was performed[10] The following case reports the outcome of multiple neurectomies followed by the insertion of multiple titanium screws into the infraorbital, greater palatine, incisive and mental foramina, which prolonged the duration of pain remission without any adverse complication.

Case Report

A 64-year-old Indian female complained of severe attack of trigeminal neuralgia at the right infraorbital and incisive papilla region.

She has been suffering from trigeminal neuralgia since 1973 i.e. for a duration of 33 years under the care of several oral surgeons. Her initial treatment was carbamazepine and dilantin sodium. She underwent neurectomy of her right infraorbital nerve the following year. This procedure relieved her pain for half a year. Since then, she has been given repeated alcohol injection and/or local anaesthetic injection over the second and third divisions of the trigeminal nerve every two to three months for the next 14 years. Intramuscular pethidine injections were able to relieve her pain when the first division of the trigeminal nerve was affected.

In 1987, her right posterior fossa was explored and selective section of the posterior third of portio major was done. This procedure stopped the pain in the third division of the trigeminal nerve but pain persisted in the second division of trigeminal nerve. A repeat peripheral neurectomy was performed on the right infraorbital nerve at its exit. She remained pain free for one year following this procedure. She continued to take carbamazepine for maintenance.

In 1991, another neurectomy was performed on her right infraorbital nerve. The surgeon observed that the nerve had re-grown when the previous surgical area was explored. She was pain free for six months, following which she resumed to carbamazepine therapy for moderate pain management.

In 1993, another right infraorbital neurectomy was performed due to recurrence of severe painful episodes. Bone wax was used to obliterate the

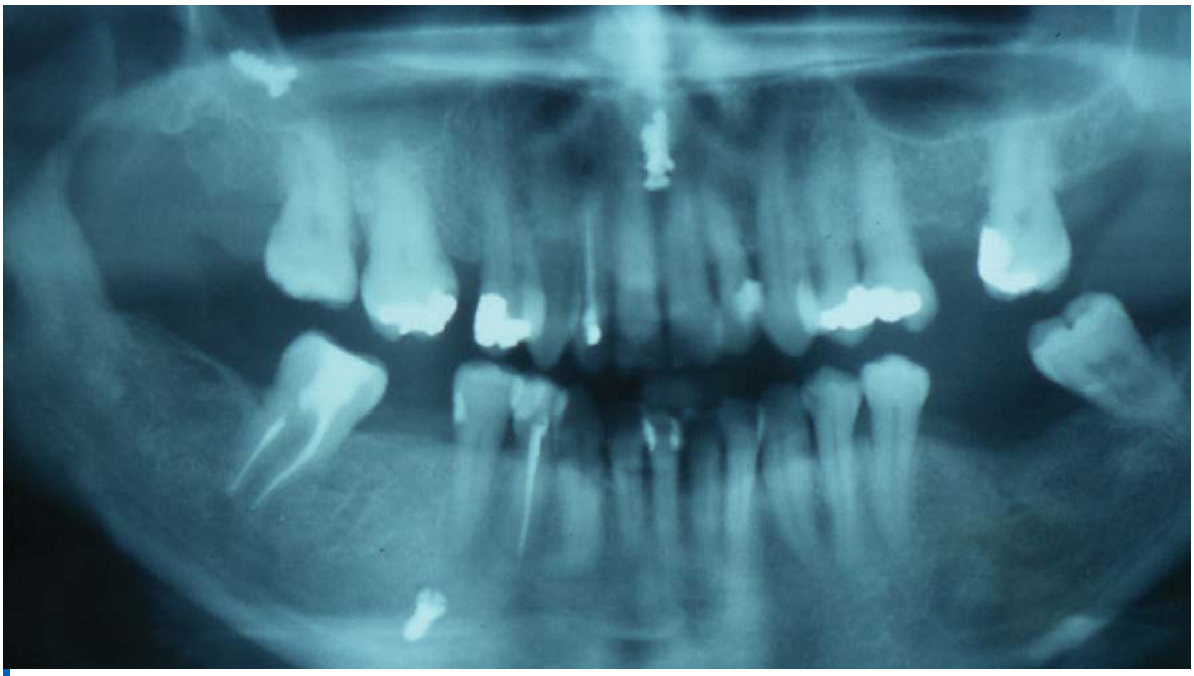

Figure 1. Orthopantomogram shows different positions of the titanium screws that were inserted into the incisive, infraorbital, greater palatine and mental foramens. Note the ghost image of a metal screw in the incisive foramen area, resulting in the appearance of having two screws in the same foramen

infraorbital foramen after nerve avulsion. This procedure relieved her pain for about a year. During this period, pain has resurfaced on the third division of the trigeminal nerve. She was referred to the Universiti Hospital Kuala Lumpur where she received 10 courses of bupivacaine (0.5%) injection, which relieved her of neuralgia for 6 months. In the mean time, she still continued with her medication of carbamazepine, where she complained of several episodes of diplopia when the dosage was increased to 800mg/day.

She was subsequently referred to the author and a senior consultant in 1993 for the management of neuralgia over the distribution of the right inferior alveolar nerve. Peripheral neurectomy of the right inferior alveolar nerve was performed in June, 1993. For about 6 months, she was free from medication. However, at the end of 1993, she reported episodes of "flick' from her right upper lip towards the tip of the nose. This became worse over one month, so the author together with the senior consultant decided to attempt cryosurgery on her right infraorbital nerve in January, 1994. She was pain free for 4 months but resumed to carbamazepine medication afterward as pain was then felt in the area supplied by the right inferior alveolar nerve. A second neurectomy of this nerve was performed in September 1994. The right inferior alveolar nerve was noted to have regenerated. Prior to that she required lignocaine and bupivacaine injections, given at home by her children (who are medical doctors) for post-operative pain control.

The following month, she experienced pain in the area supplied by the greater palatine nerve. Peripheral neurectomy of this nerve was performed with the patient under local anesthesia. Subsequently, she was able to reduce the dosage of carbamazepine to a maintenance dosage of 50 mg daily. However, in the same month, she also complained of experiencing severe pain in the area supplied by the maxillary incisive nerve. Peripheral neurectomy was performed with the patient under local anesthesia. Bone wax was place to obliterate the incisive foramen.

Three months later, she again experienced severe pain in the incisive area. Severe pain was also felt in the right infraorbital area. The pain could not be controlled even by increasing the dosage of carbamazepine to the maximum recommended dose. Besides, the patient could not tolerate the side effects of high dosage of carbamazepine. Repeat neurectomies of the right infraorbital nerve and the incisive nerve were performed with the patient under general anaesthesia. The author and the senior consultants inserted one 1.5 mm and one 2.0 mm diameter titanium screws into the infraorbital foramen and incisive foramen respectively. She was well postoperatively and needed only 50 mg Carbamazepine for maintenance.

Nine months following neurectomy, the patient again complained of severe pain in the incisive area. The surgical area was re-explored. Nerve fibers were found to have re-generated and coiled themselves around the titanium screw in the incisive foramen. The screw was tightened following the excision of overgrown nerve fibers. The patient progressed well for the next 4 years following this procedure. She has been given a low dosage (50mg daily) of carbamazepine maintenance since, but at the end of the fourth year, she started to feel

pain over the area previously innervated by the incisive nerve. Injections of plain bupivacaine 0.5% were able to provide temporary pain relief. The dosage of carbamazepine was increased to 200 mg t.d.s and this was able to control the neuralgia. Beside the right infraorbital and incisive nerves, the right long buccal and greater palatine nerves were also experiencing neuralgia, with a neurectomy done to the greater palatine nerve in 1999 and subsequent repeat neurectomy and the insertion of a 2.0 mm titanium screw under general anesthesia in 2001. The pain over the right long buccal nerve region was relieved when an endodontist performed a root canal treatment on the lower right second molar.

To conclude, the obliteration of the infraorbital and incisive foramens managed to provide adequate pain control that lasted up to 10 years. The obturation of the greater palatine foramen provided pain relief for almost 14 years. She has since developed trigeminal neuralgia over the right lateral nasal region and the right mental nerve. Root canal therapy on the lower right first premolar did not manage to provide pain relief on this occasion. A 2.0 mm titanium screw was inserted to the right mental foramen after neurectomy in 2004 (Fig. 1). She eventually underwent gamma knife surgery to control the neuralgia in 2006 and was lost to follow ups.

Discussion

Early literature revealed that there have always been two major means of treatment for trigeminal neuralgia; medical and surgical.[23] The difference with current treatment is that medical treatment in the past included topical applications of lotions, vesicants, heat, opiates, counterirritants such as plasters and blisterings, and leeches, bleeding, and purging[23], and the inhalation of trichloroethylene.[26] In the early nineteenth century, the drugs of choice included quinine sulfate, ferrous carbonate, hemlock, camphorated mercurial ointment, ether and arsenic in gruel. By the turn of the century, vitamin B and liver extracts, vasodilators, intravenous histamines, chlorpromazine, mephenesin carbamate, and cobra venom were added to the list.[23] This shows how little we understood trigeminal neuralgia until the introduction of dilantin and carbamazepine.

Carbamazepine, unfortunately, is not a miracle drug that is effective in all patients, and its effect may not be long lasting. One study assessed the long-term efficacy of carbamazepine over a 16-year period in 146 patients and reported an initial success in 60% of participants, but by 5 – 16 years only 22% of participants were still finding carbamazepine effective and 44% required additional or alternative treatment.[5] This scenario is exactly what happened to the patient in this current case. She underwent various peripheral surgical approaches to treating trigeminal neuralgia which included alcohol injection, cryotherapy and peripheral nerve avulsion (neurectomy), since she failed to fully respond to carbamazepine. Alcohol injection of the branches of the trigeminal nerve has been carried out since early 20th century[27, 28] Schlosser has been cited as the first person to advocate the use of alcohol injection[29] There are two distinct techniques to deliver peripheral injection of alcohol. In one of the techniques, a transcutaneous injection of the nerve at the skull base at the foramen ovale or foramen rotundum is performed. A second technique delivered alcohol more distally as the nerve passes recognizable foramina in the facial skeleton. Injection of alcohol (1 mL of 100% absolute alcohol), while can be easily performed, is done blindly. It is difficult to control the spread of the agent injected into the closed space.

This approach has been reported to relieve pain for an average time interval of 11-17 months[7, 30], but with a 10-39% failure rate[12, 30, 31-33] However, there will be a fall in the duration of effect with subsequent injections[26, 34] and rightly enough, such a situation was seen in the current case. Even though alcohol injections had been employed near the foramen, it did not cause permanent nerve destruction. In fact, the nerve kept regenerating, resulting in her needing re-injections every 2-3 months.

Cryotherapy, first introduced in 1976[35], has been administered with some success in this case. Cryotherapy for trigeminal neuralgia can only be applied to exposed nerve branches and not the whole divisions as is done with neurectomy. Thus, the patients' sign and symptom recurred soon after cryotherapy. Cryotherapy can provide relief of painful symptoms for about one year, as seen in this case. This is not much different from the median time to pain recurrence reported for the infraorbital (14 months), mental (9 months) and long buccal (11 months) nerves.[36] This also means that the patient still needed repeat cryotherapy. The only advantage of cryotherapy over alcohol injection and peripheral neurectomy is that there is no permanent sensory loss.

Peripheral neurectomy is not a new surgical procedure, first introduced as a treatment modality in the 18th century.[9, 12] The first comprehensive review was published by Fowler in 1886[11], and following the turn of the century, it was among the three means of treatment for trigeminal neuralgia, along with alcohol injection and ganglion root resection.[37] It is claimed to be a simple, low-risk, repeatable surgery that can be performed under local anaesthesia, as shown in this case. Post Second World War, the earliest studies were published about 50-60 years ago[9, 12, 15-17, 21-23, 30, 38], followed by sporadic publications on this mode of treatment thereafter.[18,24,39]

Cherrick[23] in presenting a case report of bilateral trigeminal neuralgia in 1972 stated that peripheral neurectomy was a very popular and successful treatment then, with very few postoperative complications. However, with the good results accorded by medical therapy and the success

of complex neurosurgical procedures such as microvascular decompression and percutaneous radiofrequency thermal rhizotomy, this mode of treatment has gradually fallen out of favor. In fact, one finding that is often overlooked by opponents of this procedure is the favorable outcome of pain relief of 5 years or more reported by Murali and Rovit in their group of patients who were first treated with radiofrequency thermocoagulation, followed by peripheral neurectomy after the recurrence of pain.[24] There have been some revivals in the last 5 years as more oral surgeons in the Indian subcontinent reported their use for treating patients who were living in the rural area and were deprived socio-economically of modern neurosurgical facilities.[7, 25, 40, 41]

Proponents of peripheral neurectomy think that this procedure still has a role to play with the elderly, medically compromised patients or those not keen to be subjected to extensive neurosurgery.[18, 24, 39]

The surgical techniques employed in this case were essentially the same as described by Hong-Sai.[10] The average pain free period achieved has been reported to be longer than that accorded by cryotherapy and lasted between 24-36 months similar to that reported by many authors.[12, 25, 30] Grantham and Segerberg[30] who electrocauterized the remaining nerve stump after performing nerve avulsion, reported to have achieved a wide range, from no improvement to pain relief up to 8 years. Yadav et al. [7] however, recently reported that 25% of their Indian patients who underwent peripheral neurectomy suffered from recurrence of neuralgia within 6 months post surgery. Another study reported a recurrence rate of 78% in patients who had undergone peripheral neurectomy during a mean follow up of 7 years. Worse, half of these patients had their first recurrence within a month[42]

Quinn and Weil reported finding bony foramina being filled with natural bone during the second and third neurectomies, with the foramina becoming smaller in size between each surgery. Hence they did not think plugging with bone or amalgam was useful as they claimed natural bone would fill these foramina up.[12]

Such an occurrence has not been observed in this case, hence the need to obliterate it with a compatible material. Hong-Sai reported that the duration of pain relief could extend up to at least 4 years in the cases where titanium screw insertion was performed.[10]

Ali et al.[41] in their prospective study found that the placement of a stainless screw into the foramen significantly increase the duration of remission. However, as their number of samples was small, and the duration of review was only 24 months, it remains to be seen if such is still the case several years later.

The insertion of a screw into a foramen following peripheral neurectomy is not new either, having been first reported by Beckmann almost one century ago.[43] Even then, he noticed that the patient with a screw inserted experienced longer remission period than others. It is believed that this case presents the longest duration of pain remission associated with the obliteration of foramina.

It has been reported that the recurrence of trigeminal neuralgia can happen at the same branch or progress to other neighboring branch(es). Yadaz et al.[7] were of the opinion that patients who have successful surgeries often need secondary or tertiary surgeries on different trigeminal nerve branches due to migration of pain. This is evident in the current case, where she experienced recurrence in the same nerve initially, and when successfully treated, migrated to other branches.

Several authors discussed the number of repeated neurectomies for peripheral nerves. [9, 24, 39]

Sung was of the opinion that peripheral neurectomy was suitable for incipient cases, and once there is a progression to other branches, intracranial surgery was preferred.[9]

Cerovic[39] reported that the remission time decreased after repetitive neurectomies.

They did not think repeating the surgery on the same nerve more than three times was of any benefit.[39]

As shown in the current case, the patient had exhausted her medical therapy of carbamazepine and all peripheral surgical treatment options, namely repeated alcohol injections, cryotherapy and repeated peripheral neurectomies. Worse, in her case recurrence happened with pain progression to the neighboring nerve branches. In accordance to the "ladder of treatment for trigeminal neuralgia", she eventually progressed to undergo intracranial surgery with apparently good outcome. It is interesting to note how resilient the trigeminal nerve can become when it has been affected by neuralgia. During repeated operations, the author and colleagues noticed that her peripheral nerves had regenerated into fine branches. This is similar to that reported by Quinn and Weil.[12, 16] It is interesting to note that within nine months following neurectomy of the incisive nerve, the nerve fiber had re-grown and coiled itself around the titanium screw in the incisive foramen. It seems as if the nerve was able to negotiate the gaps between the screw and the foramen and loosened the screw in the process of regeneration. This may also explain why bone wax was not able to block nerve regeneration.

It is known that the triggering stimulus is carried by the large myelinated axons and nociception is associated with the activation of small rnyelinated A-delta and unmyelinated C-fibers. [44]

As study has shown that small myelinated and unmyelinated nerve fibers recover faster than the larger A-alpha myelinated fibers[45], it was decided at the subsequent neurectomy that some material should be used to obliterate the foramen so that the nerve cannot regenerate to the area it originally supplied.

A titanium screw was chosen because of its biocompatibility and ease of handling. It was

placed into the foramen without the need of tapping or preparing the foramen.[10] Lastly, this case also illustrates the elusive nature of the trigeminal neuralgia that can mimic toothache. While dental extraction has been reported to provide pain relief when there is a pure odontogenic cause[46], the difficulty in differentiating between neuralgia and odontalgia may result in patients receiving inappropriate treatment, such as root canal therapy.[44] As seen in this case, such a procedure only managed to provide pain relief over the region supplied by the right long buccal nerve.

Conclusion

This case has been managed with various means of treatment since the 1970s when different modes of periphery treatment were still in use. In time, she has been in the care of several oral surgeons, at the time when neurosurgical procedure was still not easily available in the country. She might have been managed differently if she had succumbed to the same diagnosis nowadays. Having said so, this report suggests that the insertion of a titanium screw into a bony foramen can obstruct peripheral nerve regeneration, hence delaying trigeminal neuralgia from recurring.

Because of this, she is believed to be the patient with the longest duration of having a foreign body inserted into a bony foramen without any adverse effect. Perhaps in cases where peripheral neurectomies need to be done e.g. for debilitating patients etc, it may be advisable to obliterate the foramen with a metal screw.

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Wei Cheong Ngeow
BDS (Mal), FFDRCS (Ire), FDSRCS (Eng), MDSc (Mal), PhD (Sheffield), FAMM
Professor Dr. Department of Oro-Maxillofacial Surgical and Medical Sciences Surgery
Faculty of Dentistry,University of Malaya

CV

Professor Dr. Wei Cheong Ngeow is currently a lecturer at the Department of Oro-Maxillofacial Surgical and Medical Sciences, Faculty of Dentistry of the University of Malaya.
He graduated from the University of Malaya in 1992 and was a private practitioner for 9 months before he was offered the post of tutorship at his alma matter. Three years later, he went to do a house job at the Queen Victoria Hospital in East Grinstead, England.
He obtained his Fellowship in Dental Surgery from the Royal College of Surgeons in Ireland and the Royal College of Surgeons of England in 1996.
He subsequently returned to Malaysia and was a pioneer lecturer at the then newly established Universiti Kebangsaan Malaysia.
He left for private practice in 1999 but the temptation to return to academic life was greater, hence he returned to the University of Malaya the subsequent year.
He obtained a master degree in 2008 and a PhD from the University of Sheffield in 2010.
He has published over 160 articles, letters, comments and reports in both local and international journals, and was the Editor of the Malaysian Dental Journal from 2005-2007 and the Editor of the MDA Newsletter in 2015.
His research interests are craniofacial anthropometry, variations of the mandibular nerve, and recovery of peripheral nerves after microsurgical repair.

Questions

Which cranial nerve (CN) is affected in trigeminal neuralgia?

❑ a. Fourth CN;
❑ b. Fifth CN;
❑ c. Sixth CN;
❑ d. Seventh CN.

What is the target of action for dilantin and carbamazepine?

❑ a. Sodium channel;
❑ b. Calcium channel;
❑ c. Potassium channel;
❑ d. Iodide channel.

Roughly, how many percent of patients suffering from trigeminal neuralgia will end up needing surgical treatment?

❑ a. 30%;
❑ b. 35%;
❑ c. 40%;
❑ d. 45%.

Which one of these materials was popularly used by several authors to block peripheral nerve regeneration?

❑ a. Gold foil;
❑ b. Amalgam;
❑ c. Bone wax;
❑ d. Metal screw.