Factors Associated with Treatment Outcome of Carbon Dioxide Laser for Trigeminal Neuralgia

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Abstract:

Objective: To report the treatment outcome and identify factors associated with treatment outcome of using carbon dioxide (CO_2) laser neural ablation for trigeminal neuralgia (TN).

Materials and methods: This was a retrospective study of 36 patients who underwent CO_2 laser neural ablation to treat TN. The medical records were reviewed and analyzed. Pain relief for at least 1 year after the procedure would be classified as treatment success.

Results: For the total of 36 patients, 15 of them (41.7%) achieved the treatment success. Regarding the factors associated with the treatment outcome, the total daily dose of carbamazepine of 600 mg or less per day and shorter duration of symptoms prior to receiving the operation (persistent symptom of 3 years or less) were related to success of treatment. The odds ratios of both factors were 12 (95% CI = 1.6-87.9) for the carbamazepine dose, and 16 (95% CI = 2.2-112.9) for the duration of persistent symptom of 3 years or less.

Conclusions: The CO_2 laser neural ablation decreased the pain symptoms of the patients with TN. The preoperative dose of carbamazepine and the duration of symptoms prior to treatment were associated with good treatment outcomes of CO_2 laser for TN.

Keywords: Trigeminal neuralgia, Tic Douloureux, Carbone dioxide laser, Lasers

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Introduction

According to the 1st edition of the International Classification of Orofacial Pain (ICOP), trigeminal neuralgia (TN) or Tic Douloureux is defined as a disorder characterized by recurrent unilateral brief electric shock-like pain that is abrupt in its onset and termination. The pain is triggered by innocuous stimuli within the affected distribution of one or more divisions of the trigeminal nerve (1). An estimated prevalence of 0.3% was reported in the population-based study (2). In Thailand, approximately 40 patients with naive trigeminal neuralgia were reported each year at a tertiary care center (3). The peak incidence of TN was in the age range of 50-65 years and sexual predilection for female (4,5). Time-lapse before the establishment of TN diagnosis in the majority of patients was at 1 year or less. However, approximately 14.2% of patients suffered from TN since there was a further delay of up to 3 years or more before the diagnosis was made, resulting in further delay of the appropriate treatment (5).

The medication commonly used as the first-line treatment is sodium channel blocker anticonvulsant drugs; i.e. carbamazepine or oxcarbazepine (4,5). The adverse effects caused by these drugs are somnolence, postural unbalance, dizziness, liver dysfunction, anemia, leukopenia, thrombocytopenia, and allergic reactions (4,6,7). The patients that do not respond to the medical treatment, or cannot tolerate the side effects of the medications will be referred to neurosurgeons for surgical interventions including microvascular decompression, procedures targeting the Gasserian ganglion, and peripheral surgeries at neural trigger points (4). Because the peripheral procedures rarely provide pain relief beyond 1 year, these procedures are suggested for emergency use or patients whose medical problems would restrict other surgical options (8,9). Cryotherapy, peripheral neurectomy, and peripheral laser therapy are examples of the peripheral procedures.

Lasers have been introduced as an alternative or adjunctive management of TN due to their analgesic effect, safety, and considerably minimally invasive procedure (10,11). Various types of laser have been reported for the treatment of TN, including helium-neon (He-Ne) laser (12) and GaAlAs diode laser (13-15). Although the use of these lasers has many advantages, multiple sessions are required to obtain sufficient pain relief. Currently, a carbon dioxide (CO_2) laser with a 10,600 nm wavelength is also used for treating TN. Refractory or intolerance to the adverse effects of the medications and significant medical conditions of the patients, this laser has become the treatment of choice for patients who decline major surgeries, such as microvascular decompression (16, 17). After performing CO_2 laser ablation on an affected nerve, the pain is absent or promptly decreased for a certain period (17). Sessirisombat (16) reported a significant difference in pain scores between pre- and post-operation after 1 year follow-up period. However, factors associated with the treatment outcome of CO_2 laser ablation have not been reported. Thus, the purpose of this study was to report the result of the treatment and identify the factors associated with the treatment outcome of CO_2 laser neural ablation for TN.

Materials and methods

This was a retrospective study of patients who underwent CO_2 laser neural ablation to treat TN from January 2004 to December 2017 at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University. The inclusion criteria were the patients diagnosed as TN at only one branch, underwent the CO_2 laser neural ablation, and had a follow-up period of at least 1 year. The exclusion criteria were the patients with secondary TN, TN affecting more than one branch, atypical face pain, other cranial nerve neuralgia, uncontrolled systemic diseases, previous surgery for the treatment of TN, psychological problems, or pain recurrence on the other nerves. The study was approved by the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University (HREC-DCU 2019-012).

All patients underwent CO_2 laser neural ablation by the same oral and maxillofacial surgeon under local anesthesia. The surgical procedure was reported in our previous study (17). The affected nerve was identified and exposed at least 1 cm in length from the foramen via vestibular incision. Then, the nerve was ablated with a 10,600-nm CO_2 laser (Captain 30, SM Medical, Korea) in defocus and continuous mode at 5 W using a 50-mm tip for 30 sec (Fig 1). The wound was closed with resorbable sutures. Ibuprofen 400 mg tablets were prescribed for postoperative pain control. Patients were followed-up at 1 week, 1 month, and every 3-6 months after the surgery to assess the wound healing, postoperative symptoms, and the amount of carbamazepine used for postoperative neuropathic pain control.

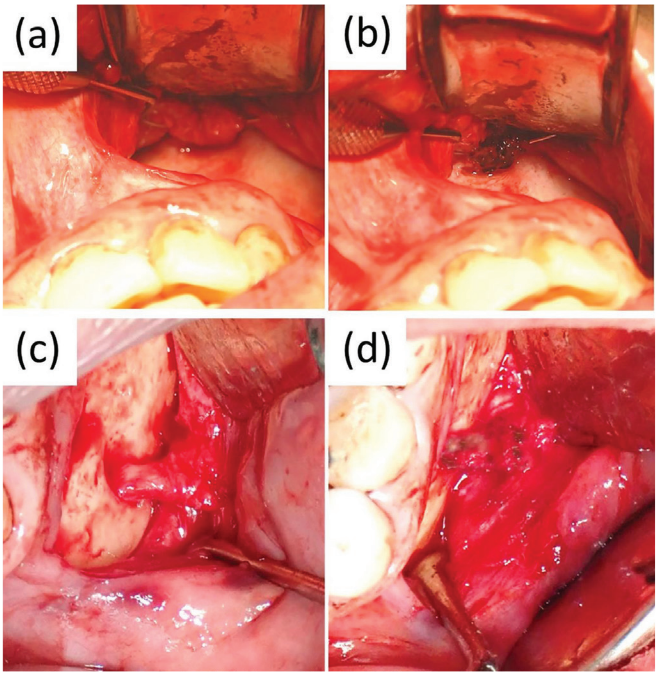

Fig 1. The surgical procedure (a) Left infraorbital and (c) left mental nerve, were identified and exposed at least 1 cm in length from the foramen via vestibular incision (b, d). The affected nerves were ablated with CO_2 laser for 30 sec.

Data were collected from medical records. The predictive variables were gender, age (≤ 60 or > 60 years), affected face side (right or left), affected trigeminal nerve division (maxillary or mandibular division), preoperative total daily dose of carbamazepine (≤ 600 or > 600 mg), and duration of symptoms before operation (≤ 3 or > 3 years). The criteria employed for treatment outcome were modified from the literature (8,15,17). The outcome variable to be recorded was the presence of pain relief, which was defined as a pain-free period without the need for carbamazepine use, or reduction of pain with at least a 50 percent decrease in carbamazepine doses compared with those preoperatively. The treatment was considered a success when the duration of pain relief of at least 1 year could be achieved.

Statistical analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM, Chicago, IL, USA). Descriptive statistics were computed to summarize the characteristics of the variables. For categorical variables, the results were reported using frequency and percentage. For continuous variables, the results were reported using mean and standard deviation (SD). The relation between the predictive variable and treatment outcome was analyzed using Chi-square test. The binary logistic regression was conducted to calculate the odds ratios (ORs) and corresponding 95% confidence intervals (CIs) of the meaningful associations of the predictive variable and expected treatment outcome. A P-value less than 0.05 was considered statistically significant.

Results

A total of 36 patients with a mean age of 61.5 ± 12.9 years were recruited in the present study (Table 1). Most patients were female (21, 58.3%) and had the pain on the right of the face (21, 58.3%). The majority of affected trigeminal division was the mandibular division (22, 61.1%), especially the mental nerve. The mean total daily dose of carbamazepine and the duration of symptoms before the operation were 675 ± 407.3 mg and 48.9 ± 48.3 months, respectively. Postoperatively, pain had been decreased for 0-62 months.

Table 1. Characteristics of the variables.

Variables (n = 36)	Overall (n = 36)	Pain relief at least 1 year after CO_2 laser	
		Yes (n = 15, 41.7%)	No (n = 21, 58.3%)
1. Age (years)	61.5 ± 12.9	62.9 ± 12.8	60.5 ± 13.2
2. Gender (%)			
- Male	41.7	16.7	25
- Female	58.3	25	33.3
3. Affected facial side (%)			
- Right	58.3	25	33.3
- Left	41.7	16.7	25
4. Affected trigeminal nerve division (%)			
- Maxillary division	38.9	13.9	25
- Mandibular division	61.1	27.8	33.3
5. Preoperative dose of carbamazepine (mg)	675 ± 407.3	526.7 ± 249.2	781 ± 467.6
6. Duration of symptoms before operation (months)	48.9 ± 48.3	26.8 ± 15.4	64.6 ± 57.4

Of the 36 patients, 15 patients (41.7%) had pain relief for at least 1 year after CO_2 laser ablation. The pain relief period of this group was 26.1 ± 17.6 months. Another group (58.3%) had pain relief less than 1 year after treatment. The pain of the second group was recured at 5.4 ± 3.2 months postoperatively.

Gender, age, affected facial side and affected trigeminal division showed no significant relation with pain relief for at least 1 year after CO_2 laser for treatment of TN (Table 2). Factors associated with this treatment outcome were the total daily dose of carbamazepine (p = 0.03) and duration of symptoms before operation (p = 0.01). After the operation, the patients with the use of carbamazepine ≤ 600 mg/day were 12 times more likely to have a pain relief period of at least 1 year compared with those with use of carbamazepine more than 600 mg/day (OR = 12, 95% CI = 1.6-87.9, p = 0.02). Moreover, the patients presented with symptoms ≤3 years potentially had pain relief at least 1 year 16 times to those with pain occurred more than 3 years (OR = 16, 95% CI = 2.2-112.9, p = 0.01).

Table 2. Factor associated with pain relief at least 1 year after using CO_2 laser for treatment of TN.

Variables (n = 36)	Pain relief at least 1 year after CO_2 laser (%)		p-value
	Yes (41.7)	No (58.3)	
1. Gender			0.86
- Male (41.7%)	16.7	25	
- Female (58.3%)	25	33.3	
2. Age			0.65
- ≤ 60 years (44.4%)	16.7	27.8	
- > 60 years (55.6%)	25	30.6	
3. Affected facial side			0.86
- Right (58.3%)	25	33.3	
- Left (41.7%)	16.7	25	
4. Affected trigeminal nerve division			0.56
- Maxillary division (38.9%)	13.9	25	
- Mandibular division (61.1%)	27.8	33.3	
5. Preoperative dose of carbamazepine			0.03*
- ≤ 600 mg/day (66.7%)	36.1	30.6	
- > 600 mg/day (33.3%)	5.6	27.8	
6. Duration of symptoms before operation			0.01*
- ≤ 3 years (61.1%)	36.1	25	
- > 3 years (38.9%)	5.6	33.3	

**Statistically significant level at $p < 0.05$.

An important postoperative complication was an alteration of sensation. Thirty-four patients (94.4%) had hypoesthesia or paresthesia after CO_2 laser. Of the 34 patients, 8 patients (23.5%) had a complete recovery from the alteration of sensation within 3–15 months postoperatively. Although most patients had some degree of prolonged neurosensory deficit, they did not realize this complication.

Discussion

Recently, there are a variety of treatment modalities for TN, both medical and surgical, to relieve and prevent episodes of pain. Treatment options are based on many factors, including patient's age, life expectancy, medical and psychiatric status, patient's compliance, and tolerability to adverse drug effects (6, 18). Blocking transmission of sensory pathways by damaging parts of affected nerve fibers or decompressing the trigeminal nerve to alleviate the pain is the main purpose of these surgical procedures (6). Due to different surgical options, the decision to select the proper one would depend on pharmacological treatment results, the patient's age, medical conditions, and surgical facilities and expertise (18). Although microvascular decompression is the first choice of surgical treatment and has a high success rate, microvascular decompression is considered the most invasive procedure for TN management (19-22). Furthermore, major complications associated with this treatment are not negligible such as cerebrospinal fluid leakage, meningitis, facial numbness and palsy (19,22).

Laser therapy is one of the surgical treatment options for TN that is classified as a peripheral procedure. This is because this technique aims to block or traumatize the peripheral branches of the trigeminal nerve distal to the Gasserian ganglion (7,18). HeNe and diode laser are used as low-level laser therapy (LLLT), or biostimulation or biomodulation, which is particularly interesting to treat neuropathic orofacial pain such as TN (12-15). Updated systematic reviews have shown that LLLT is an effective alternative method or in combination with other treatment means for TN management (10,11). This technology causes pain relief which is considered non-invasive and causes minimal side effects procedure. Possible mechanisms of analgesic effects of LLLT are reduction of the receptor sensitivity, increased pain tolerance because of changes in cell membrane potential, and shortening of the inflammatory phases (23). However, this laser treatment does not directly attack the affected nerve. The need to undergo multiple sessions to achieve the therapeutic effect is the main limitation of LLLT. Ebrahimi, et al. (14) reported that pain severity reduction decreased with time until 9 sessions of LLLT have been completed, then the gradually increasing severity of pain started at one month after the end of treatment. Finally, the pain completely recurred at 4 months after completion of treatment.

CO_2 laser ablation is later introduced as an alternative treatment for TN (16,17). In contrast to the LLLT, laser energy produced by CO_2 laser directly contact the exposed affected nerve. Consequently, immediate therapeutic effect in pain relief occurs after CO_2 laser neural ablation. The CO_2 laser is widely used in soft tissue surgery due to its affinity for water-based tissues. Heat is generated after absorption of the laser by intracellular water and results in cellular vaporization. There are three principal techniques for utilization of CO_2 laser as a surgical tool for oral surgery: incision/excision, vaporization/ablation, and hemostasis (24,25). Our study used low power laser energy to ablate a limited area of the affected branch of the trigeminal nerve to alter the sensory conduction of pain once it is stimulated to reduce, or even block the pain. This analgesic ability relates to an alteration of neural transmission and a coagulation effect on blood vessels that provides hemostasis and additionally seals the sensory nerve endings (25,26). In addition, direct damage to the nerve sheath by laser ablation disrupts the nerve function, so pain conduction is decreased (27). The nerve is partially destroyed, thus the sensation can recover. Robinson, et al. 2015 (27) showed the nerve sheath was ablated and additional damage of the nerve bundle at 5 W CO_2 laser setting that was the same power used in our study. Furthermore, some degree of nerve function impairment was also observed even with the lower power used. This mechanism could explain the analgesic effect of the CO_2 laser.

Previous studies confirmed that CO_2 neural ablation reduced pain in patients with TN (16, 17). Our result showed the range of pain relief periods was 0-62 months. Regarding the criteria of successful treatment outcome, 41.7% of the patients achieved pain relief for at least 1 year after the treatment. This was higher than the study of Eckerdal and Bastian (15) whose outcome of the treatment approximately 37.5% of the study group was considered successful after LLLT with an 832 nm diode laser at 1-year follow-up. Although most peripheral procedures usually allowed pain relief less than 1 year (8), the mean period of pain relief was 26.1 months for the group with successful treatment. However, in the group with pain relief less than 1 year after treatment, the mean pain relief period was decreased to 5.4 months.

The present study revealed there were two factors associated with the treatment outcome of the CO_2 laser for TN. Firstly, the preoperative dose of carbamazepine of 600 mg/day or less was a significant predictor for the successful treatment. Our patients who have taken low doses of carbamazepine might adjust the drug to a higher dose for pain control, however, they could not tolerate the adverse effects of the drug. They decided to undergo the CO_2 laser instead of other surgical interventions. Secondly, the duration of symptoms of 3 years or more prior to the operation was associated with poor treatment outcomes. The causes that resulted in the delay of treatment with the surgical procedures were vary. Those patients might respond to the initial therapy with carbamazepine, but eventually, unsatisfactory outcome was perceived, resulting in the prescription of even higher dose (4). Moreover, the delay of recognition and diagnosis of TN was one of the possible causes of the delay of treatment (5,28). Maarbjerg, et al. (28) reported 37% of the patients underwent dental invasive procedures because of misdiagnosis. The pain characteristic of most patients with TN was originally presented in the oral cavity, so they initially sought treatment by visiting dentists. Therefore, the dentists should be knowledgeable about the characteristics of TN to avoid maltreatment (4).

According to the results, we could use these two predictors, the preoperative dose of carbamazepine of 600 mg/day or less, and persistent pain symptoms up to 3 years or less, as two criteria to select the patient to perform the CO_2 laser ablation for the management of TN. Nevertheless, there was a limitation of this study that should be mentioned. A retrospective study design with a relatively small sample size limited the ability to generalize the results to other populations of patients with TN. Further studies using a prospective study design and increase of sample size are needed.

Conclusion

Our results showed that CO_2 laser neural ablation decreased the pain symptoms of patients with TN. The preoperative dose of carbamazepine and the duration of symptoms before treatment were associated with good treatment outcomes. The patient with the use of carbamazepine of 600 mg or less and duration of symptoms presentation of 3 years or less was a possible candidate for CO_2 laser to the treatment of TN and achieve the successful outcome at least 1 year.

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