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## ORIGINAL ARTICLE

# Management of trigeminal neuralgia. A comparison of two techniques

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**Key words:**

alcohol nerve block, cryosurgery, local anaesthesia, neurosurgical procedures, pain relief, trigeminal neuralgia

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**Abstract**

**Objectives:** Trigeminal neuralgia is a neuropathic disorder characterised by episodes of intense pain in the face. There are various treatment modalities, but none of them provides permanent pain relief. The study aims to investigate the efficacy of alcohol nerve block and cryosurgery in the treatment of trigeminal neuralgia and evaluate the outcomes in the period of 5 years follow-up.

**Methods:** A total of 108 patients presented with the features of trigeminal neuralgia were included. These individuals were treated with neurolysis therapy using peripheral ethyl alcohol injections and cryosurgery. However, only inferior alveolar nerve and the infraorbital nerve were considered for a better understanding of the outcomes. Every patient was given the treatment, alternatively.

**Results:** The results have shown that 56.5% of the patients had pain on the right side, 38% had pain on the left side and 5.6% had pain on both sides. Whereas none of the patients had pain in the ophthalmic division. The higher percentage of pain relief was in the groups using alcohol nerve block, while the higher percentage of pain relief was in the groups using cryosurgery. There were significant differences in the duration of pain relief degrees between the alcohol nerve block group and the cryosurgery group. Moreover, the duration of pain relief in the alcohol nerve block was higher than those of the cryosurgery.

**Conclusion:** The results indicated that alcohol nerve block was a better choice for trigeminal neuralgia as it gave long-lasting results and maximum patient satisfaction.

**Introduction**

Trigeminal neuralgia (TN), known as tic douloureux or classic trigeminal neuralgia, is one of the distinguished conditions in pain medicine. TN is a real source of confusion and misdiagnosis during routine dentistry, although, it is relatively rare. TN is characterised as recurrent unilateral neuropathic pain, limited to one or more divisions of the trigeminal nerve and sudden in onset and termination<sup>1,2</sup>. However, the right maxillary branch is more common, which is explained due to the narrower rotundum and ovale foramina on the right side<sup>3</sup>. The pain

characterised by intense, sharp shooting and electric shock-like pain on the face or mouth. This pain lasts for few seconds to a minute followed by a refractory period during which a new stimulation is not able to evoke another attack<sup>2</sup>.

The presence of an intraoral or extraoral trigger zone is specific as the zone provokes pain by a mechanical stimulus (chewing, drinking, shaving and applying makeup). This stimulus may lead to misdiagnosis of the pain of dental origin. The trigger zones are usually in cheek, nose, upper lip and upper teeth, it extends to the lower lip, lower teeth and chin in some people<sup>4,5</sup>.

TN may be the only major neuropathic pain that reliably responds favourably to a destructive procedure<sup>6</sup>. However, recommendations on surgical management updated by Bentsen *et al.* have not made fundamental progress. Prospective studies are needed to compare the various surgical procedures<sup>7</sup>. No definite treatment protocol for trigeminal neuralgia has been established because of its unclear aetiology; although the assumption that sclerotic superior cerebellar artery may press on the roots of the trigeminal nerve, causing neuronal discharge<sup>8,9</sup>. Furthermore, the interference of sensory stimulus with pathology in trigeminal ganglion or retrogasserian root may trigger the onset of TN<sup>6</sup>.

The treatment modalities vary from drug therapy to extracranial or intracranial surgical procedures. Surgical procedures include alcohol, phenol or glycerol injections, peripheral neurectomy of trigeminal nerve branches, rhizotomy, cryotherapy, gamma-knife radiosurgery, balloon compression of the root entry zone and microvascular decompression of the offending vascular loop<sup>10</sup>. The exemplary TN surgery should provide instant pain relief without pain recurrence and safe. Every treatment bears its benefits and drawbacks; most important of them is post-operative associated morbidity. The drug treatment continues for many months to years and bears of side effects. However, the overall of pain relief is more than 90 % and pain-free duration is more than 5 years, the posterior fossa exploration<sup>11</sup> still surgically sensitive, very expensive and bear post-operative morbidity. Certainly, all peripheral procedures are associated with early recurrence<sup>12</sup>. However, it is very important to determine which branch of the trigeminal nerve is involved. Cryosurgery gives about half the median time to recurrence as compared with alcohol injection<sup>13</sup>. Cryosurgery and alcohol nerve block are simple procedures, they not only give satisfactory pain relief, and rather they provide post-operative morbidity to an acceptable level.

There is very little information available in the literature regarding alcohol nerve block and cryosurgery, despite the fact that they are old and reliable techniques for treating TN. Based on the clinical experience, this study has evaluated the efficacy of an alcohol block and the cryosurgery of the trigeminal neuralgia irrespective of the health status of the patient. The studies conducted on the use of alcohol and cryosurgery have shown less effectiveness as compared with other surgical techniques. Therefore, this study has compared the efficacy of these two treatment modalities.

## Materials and methods

### Study design

A prospective study has been conducted on 108 patients, who were treated with neurolysis therapy using peripheral ethyl alcohol injections and cryosurgery.

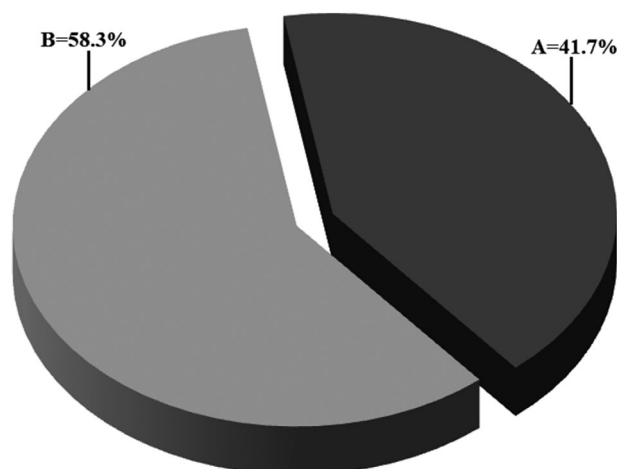
### Study participants

The patients were selected from Tertiary Hama City Hospitals in Syria from June 2005 to September 2013 with the features of trigeminal neuralgia and had been followed up for at least 5 years. All the patients were unresponsive to treatment with anticonvulsants or carbamazepine (up to 1200 mg/day) for a period of at least 3 months or the patients could not tolerate the drugs. Furthermore, none of the patients was subject to neurolytic injections or any neurosurgical treatment. Radiographs of the skull and panoramic or wide-view x-ray of the lower face were in the norm. The material divided into two distinctly different main groups according to the treatment technique;

- Alcohol nerve block group that included 45 (41.7%) patients
- Cryosurgery group that included 63 (58.3%) patients (Figure 1). Each one of the main groups was divided into two subgroups according to the trigeminal nerve branch.

### Inclusion and exclusion criteria

The basic criteria for diagnosing was based on the following features; sharp shooting, shock-like



**Figure 1** Percent of patients versus the treatment techniques; (A) Cryosurgery, (B) Alcohol nerve block.

excruciating pain, intermittent pain distributed in the division of trigeminal nerve, abrupt initiation and abrupt termination. Pain could be triggered by innocent stimuli such as touch or light and local anaesthesia cancelled the pain. The unstable medically compromised patients were not included in the study. Informed consent was obtained from participants, before recruiting them in the study.

### Informed consent and ethical approval

The patients were also informed about the advantages and disadvantages of treatment modalities. All procedures performed in this study were in accordance with the Helsinki declaration and its later amendments and with the ethical standards of the institutional and national research committee.

### Study procedure

Lignocaine blocks were given to the patients for 3 consecutive days to confirm the branch of trigeminal nerve involved. The target area was disinfected, and 1 ml lignocaine hydrochloride was injected, after a gap of 5 min, 1cc of 70% ethyl alcohol was injected slowly. Aspiration technique was applied to avoid injecting into the accompanying vessels. After an observation of 30 minutes, the patient was discharged and informed that the significant effect of injection will be after 1–2 weeks. The medications, which inhibit alcohol dehydrogenase (metronidazole, oral hypoglycaemic agents, beta-lactam antibiotics, etc.), were stopped.

Liquid nitrogen was used, when cryosurgery was applied. The target nerve was blocked first then surgically exposed. The surgically exposed nerve was frozen to  $-120^{\circ}\text{C}$  by using a thermostatically controlled temperature system for 2 minutes with the application of three cycles. Later, the interrupted sutures closed the surgical wound. Care was taken so that the cryo-probe does not come into contact with adjacent soft tissues during the procedure.

The same qualified practitioners applied the procedures, follow up and all activities related.

### Data collection

Antibiotics and anti-inflammatories were prescribed after the surgical procedure. Sutures were removed on the 5–7th post-operative day; whereas follow-up was taken after 1 and 2 weeks. There were no serious complications of applied procedures other than some facial swelling and bruising in the early post-operative period. Face-to-face questionnaire or a telephone interview was used to follow-up patients regarding duration of pain relief, outcome (talking, eating, touching, etc.) and overall satisfaction. Follow-up was performed once a month for the first 6 months and thereafter twice a year. Because sound outcome measures are needed to assess the impact of treatment interventions, we divided the patient's satisfaction level into three levels: not satisfied, satisfied and very satisfied. Furthermore, the reported patient's perception level of paraesthesia was divided into three levels: very disturbing, somewhat disturbing and disturbing but better than pain (Table 1).

### Statistical analysis

The duration of pain relief variables had five ordinal categories and patient's satisfaction level variable had three ordinal categories as well as three levels of a patient's perception of paraesthesia. Each category for each variable is assigned to a distinct numerical value, which reflects the strength of variable (Table 1). The material was analysed to evaluate if there is a relationship between patient satisfaction and his perception of paraesthesia. The data were analysed using SPSS (version 16.0; SPSS Inc., Chicago, IL, USA). Spearman's correlation coefficients were calculated.

### Results

The sample included 36 (33.3%) men and 72 (66.7%) women, with a mean age 56 (range 35–75). Forty-five (41.7%) patients had pain on the infraorbital nerve and sixty-three (58.3%) on the inferior

**Table 1** Assigned values for pain relief category, patient's satisfaction and patient's perception level of paraesthesia in the sample

Duration of pain relief category	Patient's satisfaction level	Patient's perception level of paraesthesia	Assigned value
0–1 year	Not satisfied	Very disturbing	1
1–2 years	Satisfied	Somewhat disturbing	2
2–3 years	Very satisfied	Disturbing but better than pain	3
3–4 years	–	–	4
4–5 years	–	–	5

**Table 2** Distribution according to gender, age category, involved branch, treatment location and treatment technique

Studied variable	Treatment technique	Category	N			Per cent		
			ION	IAN	Total	ION	IAN	Total
Gender	Alcohol Nerve Block	Male	7	6	13	35.0	24.0	28.9
		Female	13	19	32	65.0	76.0	71.1
	Cryosurgery	Male	15	8	23	48.4	25.0	36.5
		Female	16	24	40	51.6	75.0	63.5
	All Subjects	Male	22	14	36	43.1	24.6	33.3
		Female	29	43	72	56.9	75.4	66.7
Age	Alcohol Nerve Block	35–45 years	3	2	5	15.0	8.0	11.1
		46–55 years	11	13	24	55.0	52.0	53.3
		56–65 years	4	5	9	20.0	20.0	20.0
		66–75 years	2	5	7	10.0	20.0	15.6
	Cryosurgery	35–45 years	1	3	4	3.2	9.4	6.3
		46–55 years	17	10	27	54.8	31.3	42.9
		56–65 years	9	15	24	29.0	46.9	38.1
		66–75 years	4	4	8	12.9	12.5	12.7
	All Subjects	35–45 years	4	5	9	7.8	8.8	8.3
		46–55 years	28	23	51	54.9	40.4	47.2
		56–65 years	13	20	33	25.5	35.1	30.6
		66–75 years	6	9	15	11.8	15.8	13.9
TN Branch	Alcohol Nerve Block	Maxillary	7	8	15	35.0	32.0	33.3
		Mandibular	13	17	30	65.0	68.0	66.7
	Cryosurgery	Maxillary	30	0	30	96.8	0	47.6
		Mandibular	1	32	33	3.2	100	52.4
	All Subjects	Maxillary	37	8	45	72.5	14.0	41.7
		Mandibular	14	49	63	27.5	86.0	58.3

ION, infraorbital nerve; IAN, inferior alveolar nerve.

alveolar nerve (Table 2). Moreover, 61 (56.5%) of the patients had pain on the right side, 41 (38%) had on the left side and 6 (5.6%) had pain on both sides. None of the patients had pain in the ophthalmic division.

Each category of the duration of pain relief was analysed according to the technique used and nerve involved (Table 3). Analysis of the results in Table 3 has shown that the higher percentage of pain relief was in the group (3–4 years) using alcohol nerve block, while the higher percentage of pain relief was in the group (2–3 years) using cryosurgery.

A Mann–Whitney U test was applied to know if there were significant differences in the duration

of pain relief frequencies between the two-treatment techniques (Table 4). All P-values were much lower than 0.05. Therefore, there were significant differences in the duration of pain relief degrees between alcohol nerve block group and cryosurgery group whatever was the nerve branch at 95% of the confidence level. Table 4 has shown that the duration of pain relief in the alcohol nerve block was higher than the cryosurgery. Patient's satisfaction level is demonstrated in Table 5.

The sample divided into three categories versus the treatment technique and the trigeminal nerve branch to analyse the level of the patient

**Table 3** Duration of pain relief categories versus the treatment techniques and trigeminal nerve branch involved

Trigeminal n. branch	Treatment techniques	% of the duration of pain relief in years					Total
		0–1	1–2	2–3	3–4	4–5	
ION	Alcohol nerve block	5.0	20.0	10.0	40.0	25.0	100
	Cryosurgery	6.5	29.0	48.4	16.1	0	100
IAN	Alcohol nerve block	8.0	8.0	24.0	40.0	20.0	100
	Cryosurgery	9.4	18.8	50.0	21.9	0	100
All	Alcohol nerve block	6.7	13.3	17.8	40.0	22.2	100
	Cryosurgery	7.9	23.8	49.2	19.0	0	100

**Table 4** Mann–Whitney *U* test results, duration of pain relief frequencies, between the two-treatment techniques

Studied variable = Duration of pain relief category						
Trigeminal n. branch	Treatment techniques	<i>N</i>	Mean ranks	<i>U</i> value	<i>P</i> value	Signif. diff.?
ION	Alcohol nerve block	20	32.85	173.0	0.006	YES
	Cryosurgery	31	21.58			
IAN	Alcohol nerve block	25	35.48	238.0	0.006	YES
	Cryosurgery	32	23.94			
All	Alcohol nerve block	45	67.94	812.5	0.000	YES
	Cryosurgery	63	44.90			

**Table 5** Per cent of patient's satisfaction level versus the treatment techniques and trigeminal nerve branch

Trigeminal n. branch	Treatment technique	% of patient's satisfaction level			
		Not satisfied	Satisfied	Very satisfied	Total
ION	Alcohol nerve block	15.0	5.0	80.0	100
	Cryosurgery	12.9	9.7	77.4	100
IAN	Alcohol nerve block	0	16.0	84.0	100
	Cryosurgery	12.5	18.8	68.8	100
All	Alcohol nerve block	6.7	11.1	82.2	100
	Cryosurgery	12.7	14.3	73.0	100

satisfaction. A Mann–Whitney *U* test was applied to know if there were significant differences in the patient satisfaction level between the two treatment techniques (Table 6).

Analysis of the data shows that all *P*-values were much greater than 0.05. As a result, there were no significant differences in the patient satisfaction level between alcohol nerve block and cryosurgery whatever was the nerve, at 95% of the confidence level. All *P*-values were lower than 0.05 showing significant relationships between the patient perception level of paraesthesia values and patient's satisfaction level values whatever the technique or the nerve was in the sample (at 95% of the confidence level). Algebraic signs for calculated coefficients were positive, showing that the patient's satisfaction level increases the patient's perception level of paraesthesia as well (Table 7).

## Discussion

Currently, there are considerable modalities for the treatment of TN including the pharmacological, non-invasive and invasive techniques. Neurosurgical procedures include the lowest rates of pain recurrence, but they are sensitive, very expensive and have the highest rate of post-operative morbidity or serious complications<sup>14</sup>. Non-invasive modalities are still an actual option. For many decades, ethyl alcohol has been utilised for pain treatment resulting in a non-selective destruction of nervous tissue<sup>15</sup>. The common concentration of ethyl alcohol used for chemoneurolysis ranges from 30% to 100% solution<sup>16</sup>, but there is no determination of the minimum concentration required<sup>17</sup>. All patients included in this study were free of serious complications, despite reported complications of alcohol injection<sup>18–20</sup>.

**Table 6** Mann–Whitney *U* test results for patient's satisfaction level between alcohol nerve block group and cryosurgery group

Studied variable = Patient's satisfaction level						
Trigeminal n. branch	Treatment techniques	<i>N</i>	Mean ranks	<i>U</i> value	<i>P</i> -value	Significant diff.?
ION	Alcohol nerve block	20	26.28	304.5	0.882	No
	Cryosurgery	31	25.82			
IAN	Alcohol nerve block	25	31.76	331.0	0.140	No
	Cryosurgery	32	26.84			
All	Alcohol nerve block	45	57.54	1280.5	0.247	No
	Cryosurgery	63	52.33			

**Table 7** Spearman's correlation coefficients results. Patient's perception level of paraesthesia degrees and patient's satisfaction level according to the technique and the nerve branch

2 <sup>nd</sup> variable	Nerve	Technique	1 <sup>st</sup> variable = patient's perception level of paraesthesia			Relation significance	Relation Direction	Relation Strength
			Correlation coefficient	N	P-value			
Patient's satisfact. level	ION	Alcohol nerve block	0.470	20	0.036	YES	Positive	Medium
		Cryosurgery	0.586	31	0.001	YES	Positive	Medium
	IAN	Alcohol nerve block	0.522	25	0.007	YES	Positive	Medium
		Cryosurgery	0.670	32	0.000	YES	Positive	Medium
	Total	Alcohol nerve block	0.496	45	0.001	YES	Positive	Medium
		Cryosurgery	0.640	63	0.000	YES	Positive	Medium

Few of the previous studies have reported high rates of pain relief and high patient satisfaction with most patients' reporting<sup>21–23</sup>. A literature review accomplished by Furlan *et al.*<sup>21</sup> for limb neuropathic pain treatment reported pain relief in 44% of patients treated by chemical neurolysis. The medium duration of pain relief using ethyl alcohol injection, ranges from 6 months to more than 24 months, regardless of age, gender or repeated administration<sup>22,23</sup>. Furthermore, Ko *et al.* evaluated the efficacy and durability of internal neurolysis or "nerve combing" when neurovascular compression is not present as a treatment for TN at 1 year and 5 years. The rate of pain-free survival was 58% and 47% respectively<sup>24</sup>. However, in this study, the duration of pain relief was 3–4 years in 40% of patients. It was also 4–5 years in 25% of patients. The procedure is one of the simplest procedures with a high percentage of patient satisfaction; although, alcohol nerve block produces short to medium term of pain relief<sup>11</sup>.

Previous studies have also reported that repeated administration of ethyl alcohol does not reduce the effectiveness of this technique when the pain returns<sup>22,25</sup>. The study reported that 82.2% of patients were very satisfied with alcohol nerve blocks, irrespective of trigeminal nerve branch. The cold temperature creates neurological dysfunction that ranges from temporary conduction block to Wallerian degeneration. The nerve fibres cryoleisoned at  $-60^{\circ}\text{C}$  presented signs of freezing degeneration and create axonal damage, but leave intact the endoneurium, perineurium and epineurium<sup>26</sup>. Therefore, nerve regeneration has a structured environment for re-growth and prevented neuroma formation<sup>16</sup>.

Currently, there are limited studies, which compare the outcomes of neurolytic treatments and provide longer pain relief of TN. Results on the efficacy

of cryotherapy reported mixed results. In general, the findings of this study are consistent with the results of some other studies on pain relief<sup>27–29</sup>. These studies reported meaningful pain relief ranging from 6 to 30 months in 41–84% of the treated patients. Barnard *et al.* reported that 67% of patients were free of pain at a medium of 3 months<sup>30</sup>. Furthermore, Zakrzewska *et al.*<sup>31</sup> reported that 84% of patients experienced pain relief for 1 year<sup>27</sup>. However, this study demonstrated that the maximum duration of pain relief was 24–36 months in 49.2% of treated patients by cryosurgery irrespective of the trigeminal nerve branch. Overall, all peripheral techniques were associated with sensory loss<sup>11</sup>. However, the perception of associated paraesthesia does not affect the patient's satisfaction. This study has revealed that patient's satisfaction increases, when the perception of paraesthesia increases. In addition, peripheral techniques are useful for elderly or medically compromised patients as well as patients resistant to the drugs therapy. Undoubtedly, the invasive surgical procedures give away excellent results in the treatment of trigeminal neuralgia. Nevertheless, the management should start with drug therapy and surgical options are considered only if there is a failure to respond to medical therapy<sup>32</sup>.

## Conclusion

This has shown that peripheral alcohol injections are still useful in the management of trigeminal neuralgia, particularly in non-responsive cases to drug therapy or in patients with severe side effects or unwilling to go for neurosurgical procedures. Recurrences rates have been reported to be high in many peripheral techniques, but these procedures also have been shown to bear the lowest morbidity in refractory patients to medical therapy or in patients who are unable to undergo neurosurgical treatment.

Moreover, cryosurgery of trigeminal nerve produces a reliable, prolonged pain relief with no aggravation of symptoms. It is a simple procedure for those patients who want to avoid major surgery. This study results are limited because it lacks knowledge about drug use after the procedure and the perception of patients were not evaluated; therefore, the results are quite simplified. The study has also not measured the level of pre-operative pain. Moreover, no diagnostic examination (especially MRI) was performed for excluding secondary forms of trigeminal neuralgia.

### Clinical implications

Higher percentage of pain relief was in the groups using alcohol nerve block; while the higher percentage of pain relief was in the groups using cryosurgery.

The duration of pain relief in alcohol nerve block was higher than cryosurgery.

The alcohol nerve block was a better choice for trigeminal neuralgia as it gave long-lasting results and maximum patient satisfaction.

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