Comparison of Cryosurgery and Peripheral Glycerol Injection in Treatment of Trigeminal Neuralgia

ASFAR HUSSAIN¹, ASIF NAZIR², NADIA BASHIR³, BASHIR AHMED JALBANI⁴, ABU TALIB NOORANI⁵, SAJID HUSSAIN⁶ ¹Lecturer Oral and Maxillofacial Surgery Department Bibi Aseefa Dental College, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana.

²Associate Professor of Oral and Maxillofacial Surgery Department, Nishtar Institute of Dentistry, Multan.

³Lecturer Operative Dentistry Department, Bibi Aseefa Dental College, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana.

⁴Assistant Professor Oral and Maxillofacial Surgery Department, Bibi Aseefa Dental College Shaheed Mohtarma Benazir Bhutto Medical University, Larkana. ⁵Postgraduate resident at Oral and Maxillofacial Surgery Department. Jinnah Postgraduate Medical Center, Karachi.

⁶Post graduate resident at oral and maxillofacial Surgery Dept. Institute of dentistry, LUMHS, Jamshoro.

Correspondence to: Asfar Hussain, Email: asfargio@gmail.com, Cell: 03003001402

ABSTRACT

Background: Trigeminal neuralgia (TN) is a unique debilitating ailment due to its typical symptoms and wide array of surgical treatment modalities available for TN and it is important to select the most appropriate surgical procedure.

Aim: To compare the efficacy of peripheral glycerol injection and cryosurgery in the remission of pain in the treatment of trigeminal neuralgia.

Methodology: A randomized controlled trial (RCT) study was started after taking ethical approval, total of 80 patients of both gender were included in this study at Department of Oral and Maxillofacial Surgery, Nishtar Institute of Dentistry Multan from July 2017-January 2018. Patients were divided in two equal groups randomly, group A was treated with peripheral glycerol injection and group B with cryosurgery. Patients were followed up for 3rd month to evaluate the efficacy. All results were entered and analyzed in SPSS 24 version. Outcome variables were presented as mean and SD and qualitative variables were presented as frequency/percentages. Probability value ≤ 0.05 was considered as significant.

Results: The efficacy of cryosurgery was observed as (75%), while the efficacy of anhydrous glycerol was noted as (37.5%). This study results support the cryosurgery rather than peripheral glycerol injection in the treatment of trigeminal neuralgia as cryosurgery has higher efficacy and low recurrence rate in controlling pain than peripheral glycerol injection. Efficacy in both groups with age in 40-65 years (p=0.003) was significant. Efficacy in both groups with type of nerve in mental nerve (p=0.030) and inferior alveolar (p=0.039) were significant and infraorbital (p=0.197) and lingual nerve (p=0.386) were not significant. **Conclusion:** Our study results were supported to the cryosurgery rather than the injection of peripheral glycerol for treatment of

trigeminal neuralgia. **Keywords;** Trigeminal Neuralgia, Peripheral Glycerol injection, Cryosurgery.

INTRODUCTION

Trigeminal neuralgia (TN) is a serious health problem of orofacial region, characterized by sharp, lancinating, stabbing, electric current like paroxysmal pain, which lasts for few seconds to less than two minutes¹⁻³. Pain is unilateral in 97% patients⁴. Pain may be evoked by some non-noxious stimuli like chewing, swallowing, cold, light touch or any kind of movement⁵⁻⁶. There is refractory period between the attacks, but some patients have dull ache or paresthesia⁷. Female to male ratio is greater. It has annual incidence of 4-13/ 100,000 and increases with age and rare below 40 years^{4, 8}. The proper etiology regarding TN is unknown. But the majority of studies suggest demyelination of nerve because of compressed nerve by vessels, tumors, or due to multiple sclerosis⁴⁻⁶.

First line of therapy in the management of TN is medicine e.g. carbamazepine⁹⁻¹⁰. Other treatment options are microvascular decompression, glycerol rhizotomy, radiofrequency rhizotomy, peripheral neurectomy, peripheral glycerol injection, cryosurgery, phenol injection and alcohol injection^{7, 11}. In previously conducted studies the efficacy of anhydrous glycerol was 44% and the efficacy of cryosurgery was 77% ^{4, 12}.

Although various surgical and non-surgical techniques are used to treat trigeminal neuralgia but there is no consensus on algorithm and there is scanty literature regarding comparison of cryosurgery and peripheral glycerol injection. So purpose of this study was to determine the efficacy of peripheral glycerol and cryosurgery.

METHODOLOGY

A randomized controlled trial (RCT) study was started after taking ethical approval from ethical committee of local institute. Written consent of the patients was taken after explaining study protocol.

This study was conducted from July 2017 to January 2018 at Department of Oral and Maxillofacial Surgery, Nishtar Institute of Dentistry Multan. Total 80 patients were recorded with nonprobability consecutive sampling technique. Inclusion criteria were as patients of both genders having age from 40 to 80 years having trigeminal neuralgia of maxillary and mandibular branch of trigeminal nerve only. Patients who were not responding to medicine even after taking 1500 mg of carbamazepine per day. Patient who were allergic to medicines, or had severe / intolerable side effects. Exclusion criteria were as TN due to known secondary causes e.g. stroke, systemic sclerosis, multiple sclerosis, trauma, brain tumors. Patients previously treated by peripheral neurectomy. Medically compromised patients like known bleeding diathesis, diabetic and hypertensive. Patients who were not willing to be part of this study were excluded.

Patients were diagnosed through history, clinical examination, and relief from carbamazepine. Diagnostic criteria according to history was as; Paroxysmal attacks of pain lasting from few seconds to less than two minutes that affect one or more divisions of the maxillary and mandibular branches of trigeminal nerve. Pain has at least one of the following characteristics intense, sharp, superficial, or stabbing precipitated from trigger areas or by trigger factors. Attacks were similar in individual patients. Pain not attributed to another disorder.

Local anesthetic block for each nerve was given to locate the affected branch of trigeminal nerve. A predesign proforma was used for collection of patient's demographic details like name, gender and age. Patients were divided into two groups by using odd and even method i.e. group A with odd numbers and group B with even numbers. In both groups standard intraoral injection containing 2% lidocaine and 1:100000 epinephrine was given to identify the nerve by consequent abolition of pain. In group A 1 ml of peripheral glycerol was injected to affected nerve and in group B cryosurgery was performed for treatment of trigeminal neuralgia. In cryosurgery technique affected nerve was exposed using intraoral incision. The affected nerve was freezed with thermostatically controlled temperature of -120 Cº. The cycle of 2 minutes freeze, followed by 5 minutes of thaw was performed three times. All patients undergoing cryosurgery were advised to rinse with 0.12% chlorhexidine gluconate. Efficacy was assessed by clinical examination on the 7th postoperative day, after 8 weeks and 3

months. Data were entered and analyzed with SPSS version 24 for calculation of mean and standard deviation for the age and duration of trigeminal neuralgia. Frequencies and percentages were computed for categorical variables like gender, age groups, type of nerves involved and efficacy in both treatment groups. Efficacy in both groups was compared by applying chi-square test at level of significance with p-value ≤ 0.05 .

RESULTS

There were 75% males and 25% females in each group A and B. There were 80% patients between 40-65 years and 20% between 66-80 years of age in group A while in group B 85% patients between 40-65 years and 15% between 66-80 years of age. Table. 01. Visual analogue scale was noted as no pain in 37.5%, mild pain 27.5%, moderate 12% and severe 22% patients for anhydrous glycerol treated patients. While, for cryosurgery patients, visual analogue scale was noted as no pain in 72.5%, severe 7.5%, and mild pain 5%. Table. 02. Efficacy in both groups with male (p=0.032) and female (p=0.018) was significant. Table. 03 Efficacy in both groups with age in 40-65 years (p=0.003) was significant. Efficacy in both groups with type of nerve in mental nerve (p=0.030) and inferior alveolar (p=0.039) were significant. Table. 04.

Table-1. Descriptive statistics of Gender and Age groups.

Characteristics	Group a		Group b	
	Frequency	Frequency % Frequ		%
Gender (n = 80)				
Male	26	65.0 30		75.0
Female	14	35.0	10	25.0
Age groups				
40-65 years	32	80.0	34	85.0
66-80 years	8	20.0	6	15.0

Table-2. Association of Efficacy with visual analogue scale.

visual analogue Groups		Efficacy		P-value
scale		Yes	No	
		n=44	n=36	
No pain	Group A	15	-	-
n=44	Group B	29	-	
Mild	Group A	-	11	-
n=13	Group B	-	2	
Moderate	Group A	-	5	-
n=11	Group B	-	6	
Severe	Group A	-	9	-
n=12	Group B	-	3	

Table- 03. Association of Efficacy with gender

Gender	Groups	Efficacy		P-value
		Yes	No	
		n=44	n=36	
Male	Group A	10	16	0.032
n=56	Group B	21	9	
Female	Group A	5	9	0.018
n=24	Group B	8	2	

Table-4. Association of Efficacy with type of nerve.

Туре	Groups	Efficacy		Total	P-value
		Yes	No	with %	
		n=44	n=36		
Mental nerve	Group A	5	9	14 (35%)	0.030
n=30	Group B	12	4	16 (40%)	
Inferior	Group A	6	12	18(45%)	0.039
alveolar	Group B	11	5	16(40%)	
n=34					
Infraorbital	Group A	2	4	6(15%)	0.197
nerve	Group B	3	1	4(10%)	
n=10					
Lingual nerve	Group A	1	0	1(2.5%)	0.386
n=3	Group B	1	1	2(5%)	
Buccal nerve	Group A	1	-	1(2.5%)	NA
n=3	Group B	2	-	2(5%)	

DISCUSSION

The alleviation of pain involves one of the major services rendered by healthcare professionals engaged in delivery of health services which is specifically true when one talks about the pain as excruciating as trigeminal neuralgia. It is unique type of chronic pain syndrome for its symptoms, high burden of disease which responds to anticonvulsant medications, particularly carbamazepine¹³.

The exact cause and the pathology of the trigeminal neuralgia is still controversial. Mechanical factors like tentorial ossification, vascular compression by the superior cerebellar, anterior inferior cerebellar and basilar artery and arteriovenous malformation of the cerebellopontine angle, compression by tumors and multiple sclerosis are considered as possible causes⁴⁻⁶. However, the definite cause of trigeminal neuralgia is still not determined therefore there is no treatment which will absolutely cure the patient¹⁴.

Trigeminal neuralgia responds well to anticonvulsant medication, particularly carbamazepine. Medical treatment becomes intolerable or refractory over a period of time in 50% of the patients¹⁵. Others invasive procedures are useful for managing the trigeminal neuralgia include peripheral glycerol, cryotherapy, peripheral neurectomy, radio-frequency thermo-coagulation and microvascular decompression of the trigeminal nerve root. All these procedures have potential adverse effects, and may not be suitable for all patients¹⁶.

Hakanson S first injected anhydrous glycerol into trigeminal cistern in 1981¹⁷. Since then glycerol has been reported to be effective in the treatment of trigeminal neuralgia. To avoid possible complications of central injection¹⁸⁻¹⁹. Peripheral injection into the different affected nerves introduced by Stajcic Z¹⁴ and structural changes in the nerve fibers after glycerol injection was reported by Lunford et al¹⁹.

In our study patients treated with peripheral anhydrous glycerol had mean age of 56.40±10.23 years. There were 80% patients between 40-65 years and 20% between 66-80 years of age. While, the mean age of patients of the cryosurgery treated patients was 57.77±9.04 years. There were 85% patients between 40-65 years and 15% between 66-80 years of age. Supporting our study, Han et al, in his study described mean age 61.3 years range, 17-91 years²⁰. In another study Shah et al., ²¹ described a slightly raised age of patients 40-79 years with mean age of 59.5 years which is also in compliance to our study. Salama et al., ²² in their study described the mean age of the patients presented with trigeminal neuralgia was 50.9 ± 7.75 years with range of 40-70 years in group 1 and a mean age of 53.3 ± 8.87 years in group 2. So it is concluded that mean age range disease between 50 - 60 years. Hence trigeminal neuralgia is more common in elderly patients.

In our study there were n=26 (65%) males and n=14 (35%) females in group A (patients treated with peripheral glycerol) and there were n=30 (75%) males and n=10 (25%) females in group B (patients treated with cryosurgery). On the contrary to Salama H et al., 22 described in his study there were male = 13 (61.9) and females =8 (38) in group 1 and there were n=9 (60%) male and n= 6 (40%) female in group 2. Our results have higher ratio of male patients, this may be due to the cultural or traditional variation females have less access to health that's is why our results have higher male to female ratio.

In patients treated with anhydrous glycerol (group A), types of nerve involved observed as mental nerve n=14 (35%), inferior alveolar n=18 (45%), infraorbital nerve n=6 (15%), lingual nerve n=1 (2.5%) and buccal nerve n=1 (2.5%). In patients treated with cryosurgery (group B), types of nerve involved observed as mental nerve n=16 (40%), inferior alveolar n=16 (40%), infraorbital nerve n=4 (10%), lingual nerve n=2 (5%) and buccal nerve n=2 (5%). Supporting our results Sohail et., ⁴ all, in his study reported mental nerve (44%), inferior alveolar nerve (18%), infraorbital nerve (30%), lingual nerve (2%), long buccal nerve (6%).

Our study also indicated the distribution of duration of disease as between 1-10 years for n=32 (80%) patients and 11-20 years for n=8 (20%) patients. While Han et al., ²⁰ describes the mean duration of disease in his study as 71.4 months (5.9 years), which is also support our study.

Alam J et al., ¹² reported the efficacy of cryosurgery as 76.6% which is comparatively similar to our results in study as 75%. While another study described lower efficacy cryosurgery as 41%¹⁰. Efficacy of peripheral glycerol injection was 37% in our results. In compliance to our results Sohail A et al., ⁴ in his study described the efficacy of peripheral glycerol as 44%. While Santosh et al., ¹⁶ in his study reported the 14 patient got relief from pain out 30 which is slightly higher efficacy as it is 46.6% comparative our results.

CONCLUSION

Our study results were supported the cryosurgery rather than the injection of peripheral glycerol for treatment of trigeminal neuralgia as cryosurgery had higher efficacy and low recurrence rate in controlling pain than peripheral glycerol injection. All the practitioners treating such patients should always employ cryosurgery to avoid recurrence in such patients which may improve quality of life of these patients.

REFERENCES

- Melek LN, Devine M, Renton T. The psychosocial impact of orofacial pain in trigeminal neuralgia patients: a systematic review. International journal of oral and maxillofacial surgery. 2018 Jul 1;47(7):869-78.
- Babu A, Babu AK, Chitkara N, Joshi R, Malik R, Jangir P. Trigeminal Neuralgia: A Review. International Healthcare Research Journal. 2017 Jul 1;1(4):9-14.
- Araya EI, Claudino RF, Piovesan EJ, Chichorro JG. Trigeminal neuralgia: basic and clinical aspects. Current neuropharmacology. 2020 Feb 1;18(2):109-19.
- Sohail A, Saeed M, Qazi MR. Efficacy of glycerol injection in the management of trigeminal neuralgia. Pak Oral Dent J. 2006;26(01):93-6.
- Gaweda A, Jach E, Tomaszewski T. Different treatment methods in a patient with idiopathic trigeminal neuralgia. J Preclin Clin Res. 2011;1:35-7.
- Alssop JM, Twiddy M, Grant H, Czoski-Murray C, Mon-Williams M, Mushtaq F, Phillips N, Zakrzewska JM, Pavitt S. Diagnosis, medication and surgical management for patients with trigeminal

neuralgia: a qualitative study. Acta neurochirurgica. 2015;157(11):1925-3.

- Punyani SR, Jasuja VR. Trigeminal neuralgia: An insight into the current treatment modalities. J Oral Biol Craniofac Res. 2012;2(3):188-97.
- Benetto L, Patel NK, Fuller G. Trigeminal neuralgia and its management. Br Med J. 2007;334(7586):201-5.
- Bendtsen L, Zakrzewska JM, Heinskou TB, Hodaie M, Leal PR, Nurmikko T, et al. Advances in diagnosis, classification, pathophysiology, and management of trigeminal neuralgia. The Lancet Neurology. 2020 Sep 1;19(9):784-96.
- Zakrzewska JM. Cryotherapy in the management of paroxysmal trigeminal neuralgia. J Neurol Neurosurg Psychiatry. 1987;50(4):485-7.
- Alshaikh JT, Sudhakaran S, Rubeiz H. Trigeminal Neuralgia. Pain Management: A Problem-Based Learning Approach. 2018 May 1:7.
- Alam J, Channar KA, Khoso NA, Warriach RA, Memon AB. Comparison of pain relief after cryosurgery and peripheral neurectomy in management of trigeminal neuralgia. J Pak Dent Assoc. 2012;21:242-7.
- 13. Rappaport ZH. The choice of therapy in medically intractable trigeminal neuralgia. Isr Med Sci. 1996;32:1232-4.
- Stajcic Z. Peripheral glycerol injections in the treatment of idiopathic trigeminal neuralgia. Int J Oral Maxillofac Surg. 1989;18:255-7.
- Al-Kateeb TL. Morphological effects on the mental nerve. Oral Surg Oral Pathol. 1998;85:248-51.
- Santosh BS, Shivamurthy DM, Mangalekar SB, Thippeswamy SH, Shetty R, Singh JR. Management of trigeminal neuralgia with peripheral glycerol injection: A clinical study. J Adv Med Dent Sci Res. 2016;4(1):135-8.
- Hakanson S. Trigeminal Neuralgia treated by the injection of glycerol in the Trigeminal Cistern. Neurosurgery. 1981;9(6):638-41.
 Khandeparker RVS, Kiran S, Jain H, Berval V. Management of
- Khandeparker RVS, Kiran S, Jain H, Berval V. Management of Trigeminal Neuralgia: A Review on Peripheral Surgical Interventions. Med Res Chron. 2015;2(3):430-40.
- Lunford LD, Bennet MH, Martinez AJ. Experimental Trigeminal Glycerol injection; electrophysiologic and morphologic effects. Arch Neurol. 1989;42(2):146-49.
- Han KR, Chae YJ, Lee JD, Kim C. Trigeminal nerve block with alcohol for medically intractable classic trigeminal neuralgia: long term clinical effectiveness on pain. Int J Med Sci. 2017;14(1):29-36.
- Shah SA, Khattak A, Shah FA, Khan Z. The role of peripheral neurectomies in the treatment of trigeminal neuralgia in modern practice. Pak Oral Dent J. 2008;28(2):237-40.
- Salama H, Ben-Khayal H, Mohamed MAS, El-Mitwalli A, Zaher AA, Ezzeldin A, Ezzeldin A, Badr H, Vorkapic P. Outcome of medical and surgical management in intractable idiopathic trigeminal neuralgia. Ann Indian Acad Neurol. 2009;12(3):173-8.