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Research Article

Efficacy of Gamma Knife Stereotactic Radiosurgery in the Treatment of Primary Trigeminal Neuralgia

Zaki Noah Hasan[1], Bassam Mahmood Flamerz Arkawazi[1*], Ahmed Mohammed Mostafa[2], Mohammed Asaad Albayaty[1]

[1] Al-Kindy college of medicine, University of Baghdad, Baghdad, Iraq
[2] Saad Alwitry neurosciences hospital, Baghdad, Iraq
* Corresponding author's email: bassamarkawazi@kmc.uobaghdad.edu.iq

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ABSTRACT

Background: Trigeminal neuralgia (TN), or Tic Douloureux, is one of the most common neuropathic pains. Gamma knife stereotactic radiosurgery (GNSRS) has been considered one of the procedures for treating primary TN.
Objective:
This study evaluates the effectiveness of GNSRS in treating primary TN in patients who are unresponsive to medical treatment in a single-center experience.
Subjects and Methods: This study was conducted on 180 patients from January 2018 to October 2021. The study utilized the Barrow Neurological Institute (BNI) pain intensity score to assess pain before and after GNSRS treatment.
Results: A total of 180 patients with primary TN were included in this study, 108 females with a 1.5:1 female: male ratio. significant pain score reduction post-GNSRS, indicating GNSRS as an effective second-line treatment for primary TN was recorded. The study suggests GNSRS's potential in decreasing medication dosage with minimal short-term complications, recommending further research to assess long-term benefits and side effects. A notable decrease in medication usage was reported, with minimal short-term complications. These results support the consideration of GNSRS as a viable alternative for TN patients who have exhausted traditional treatment options. Further research is recommended to explore long-term outcomes and potential side effects associated with GNSRS.
Conclusions: The study's findings demonstrate that GNSRS is an effective and safe second-line treatment for patients with primary TN unresponsive to medical therapy. Significant reductions in pain intensity, as measured by the BNI pain scale, were observed following GNSRS treatment.

Introduction

TN was first described in the second century by Aretaeus of Cappadocia, a contemporary of Galen; the first article was published in 1773 by John Fothergill, who presented it to the Medical Society of London. (1,2) The prevalence of TN in the general population is 0.7 per 100,000. (3,4) When introduced in 1962, Carbamazepine, an anticonvulsant, was shown to be effective for patients with TN. Since then, anticonvulsants have played a crucial role in pharmacological treatment. (5) Recently, as a new modality of management, GKR

has been effective for patients with TN. (6) The procedure is performed by applying a high dose of a focused beam of radiation at the trigeminal root entry zone, which, over time, causes axonal degeneration and necrosis and thus interrupts pain signals. (7) GNSRS has many advantages over other surgical procedures, like microvascular decompression (MVD), as it is noninvasive, making it a possible substitute for patients having co-existent medical conditions, on anticoagulants or those refusing to take anticonvulsants. (8,9) However, limitations of using GNSRS may include facial numbness (which affects approximately 10% of the treated patients) and the high cost of the procedure. (10,11) Moreover, permanent dysesthesias and anesthesia Dolorosa negatively impact the quality of life, which have been reported in a limited number of patients. (12) Furthermore, pain reduction is frequently delayed for an average of one month after GNSRS. As a result, some authors recommend that patients with severe pain who require immediate relief should undertake other modalities of management. (12,13)
This study aimed to assess the effectiveness of GNSRS in patients with primary TN who show failure or suboptimal response to medical treatment.

The primary objective of this study is to evaluate the effectiveness and safety of GNSRS as a second-line treatment for patients with primary TN who have not responded to conventional medical therapy. Specifically, the study aims to determine the extent to which GNSRS can reduce pain intensity, as measured by the BNI pain scale, and to assess the impact of GNSRS on medication reduction and short-term complication rates in this patient population.

Subjects and Methods

This study is a prospective cohort study, where a group of patients with primary TN unresponsive to medical therapy were followed over time to assess the outcomes after GNSRS. This approach was chosen to observe the longitudinal effects of GNSRS on pain intensity, medication usage, and safety profiles in a real-world setting, providing valuable insights into the long-term efficacy and safety of this treatment modality One hundred eighty patients with primary TN with failure or suboptimal pain relief despite adequate medication. They were referred to the GNSRS Center at Saad Alwitry Neurosciences Hospital with a confirmed primary TN diagnosis. Each patient was selected according to the International Classification Headache Disease ICHD-3/2018. The pain was assessed using the BNI pain score before and after GNSRS. Each patient was followed monthly for three months to one year (mean = 8.22 months) after GNSRS. Data collection extended over the period from January 2018 to October 2021.The treatment procedure was applied by GNSRS using Gamma Knife Perfexion, Elekta. One isocenter 4 mm from the brainstem targeting the trigeminal nerve entry zone via a 4 mm collimator window. The target dose was 80 Gy for all patients.

Patients with facial pain due to primary TN meet (ICHD-3 Criteria for Trigeminal Neuralgia and Classical Trigeminal Neuralgia) with no other neurological disorders taking Carbamazepine or Ox carbamazepine in maximum dose plus a maximum dose of Baclofen plus a maximum dose of Gabapentin, Topiramate, or Pregabalin were included in the study. In contrast, patients with secondary causes of TN, abnormal brain imaging, who received previous GKR, with atypical facial pain, or with previous MVD surgery for TN were excluded. Statistical Package for Social Sciences (SPSS) version 20 was used for statistical analysis. Descriptive statistics are presented as scores and frequencies as percentages. Fisher's exact test used p-values, and test statistics were provided by these functions. A low p-value (typically <0.05) suggests a statistically significant difference between pre-and post-treatment outcomes.

Results

A total of 180 patients with primary TN were included with age range 36-72 years (mean= 52.8±10.8 years); 12 (6.7%) of them were less than 40 years, 45 (25%) of them were 40-49 years, 57 (31.7%) of them were 50-59 years, 51 (28.3%) of them were 60-69 years, and 15 (8.3%) of them were 70 years and more. 108 of the patients were female with a 1.5:1 female: male ratio.
The TN was right sided in 120 (66.7%) patients and left sided in 60 (33.3%) patients. TN distribution was ophthalmic in 12 (6.7%), maxillary in 72 (40.0%), mandibular in 36 (20%), and maxillary with mandibular in 60 (33.3%) of the patients. BNI pain score before GNSRS was 4 in105 (58.3%) of patients and 5 in 75 (41.7%) of patients.
By the end of the follow up, the BNI pain scores after GNSRS were 1 in 87 (48.3%) patients, 2 in 15 (8.3%) patients, 3 in 60 (33.3%), 4 in 15 (8.3%) patients, and 5 in 3 (1.7) (table 1).

Table 1: Pain characteristics BNI sores changes before and after GNSRS

BNI pre-GKR	Number (%)	BNI post-GNSRS	Number (%)	P value
1	0	1	87 (48.3)	0,04418* Using fisher exact test Statistically significant
2	0	2	15 (8.3)	
3	0	3	60 (33.3)	
4	105 (58.3)	4	15 (8.3)	
5	75 (41.7)	5	3 (1.7)	
Total	180 (100)	Total	180 (100)	

Table 1 illustrates the significant reduction in BNI scores following GNSRS treatment. It highlights that a majority of patients BNI scores where changes from 4,5 scores to 1,2,3, scores, which is an important indicator of the efficacy of GNSRS in treating primary TN (p value =0,04418* Using fisher exact test Statistically significant).
Medication after GNSRS was stopped in 102 (56.7%) patients, and reduced dose in 60 (33.3%) patients, and only 18 (10%) patients kept on same dose of medication (table 2).

Table 2: medication change percent post-GNSRS

Patient Group	Pre-GNSRS Medication Usage	Post-GNSRS Medication Usage	Change in Medication Usage
Stopped Medications	0 (0%)	102 (56.7%)	102 patients stopped medications
Decreased Dose	0 (0%)	60 (33.3%)	60 patients decreased dose
Same Dose	180 (100%)	18 (10%)	162 fewer patients on the same dose
Total Patients	180 (100%)	180 (100%)	

Table 2 illustrates the significant reduction in medication usage following GNSRS treatment. It highlights that a majority of patients were able to either stop or reduce their medication, which is an important indicator of the efficacy of GNSRS in treating primary TN.

Discussion

In current study, the mean age of the patients was 52.8 years with predominance of age group 50-59 years (31.7%). This finding is close to the results by Bangash TH study, which reported that the mean age of patients with TN was 54 years. (14).

Our study showed predominance of female gender for TN patients (female: male ratio = 1.5:1). This agree with De Toledo et al. (15) a systematic review study from multiple countries, who found that women older than 40 years had higher prevalence of TN than men, and consistent with the results of Al-Quliti KW's (16) study, Al-Khafaji ZA study (17), and are also similar to results of Siqueira et al (18) study which found that TN was more prevalent among elderly age women. The predominance of female gender with TN is due to long expectancy of life for women compared to men and TN is a disease of elderly population. (19).

Additionally, our current study showed TN was more common on the right side (120 patients, 66.7%) than on the left side (60 patients, 33.3%); a finding was similar to the results of Toda K, who stated that 66% of cases with TN were on the right side. (20) Santo Neto H, Camilli JA, Santo Neto H, Camilli JA, and Marques MJ reported that the right side's smaller foramen rotundum and foramen ovale accounted for the higher incidence of right pain distribution in their study. (21).

The TN distribution was mainly maxillary in 72 (40%) patients, maxillary and mandibular in 60 (33.3%) patients, mandibular in 36 (20%) patients, and ophthalmic in 12 (6.7%) patients. These findings agree with the results of Piagkou et al. study, which documented that pain distribution of TN is variable between patients but with predominance in maxillary and mandibular. (22) However, other study by Tuleasca et al found that TN pain distribution was concentrated for maxillary and maxillary and mandibular. (23) The pain distribution is dependable on pain threshold for patients in each study and interpretation facilities of pain in addition to variability in treatment history.

Before applying GNSRS, The BNI pain score in this study was 5 in 105 (58.3%) and 4 in 75 (41.7%); these findings were consistent with the Karam et al. study, which reported a higher pain score for patients with TN. (24).

In this study, following GNSRS, 102 (56.7%) patients stopped the medication, 60 (33.3%) patients had reduced the dose of medication, and only 18 (10%) patients kept on the same dose of medication; these findings coincide with the results of the Young et al. a study that revealed a reduction in medication use was significantly accompanied the use of GNSRS for patients with TN. (25) However, our results regarding medications are better than the results of Knafo et al study which found that only 34.3% of the patients with TN discontinued the medications after the application of GNSRS. (26) Régis et al. reported that radiosurgery outcomes for patients with TN were mainly pain reduction, decreased continuing on medications, and high patient satisfaction. (27).

There was a highly significant decline in pain scores post-GNSRS compared to pain scores pre-GNSRS; this is consistent with other series by Faraj et al. and Tempel et al., which revealed significantly reduced pain scores for patients with TN following treatment with GNSRS. (28,29).

Comprehensive data collection over a significant period, utilization of the BNI pain scale, a reliable tool for assessing pain in trigeminal neuralgia, and inclusion of a considerable number of patients all enhanced the study's statistical power and added strengths to the study.

However, the following points were encountered as limitations: The Absence of a control group limits the ability to attribute improvements solely to GNSRS. Additionally, there is a potential for selection bias, as patients unresponsive to medical treatment might have distinct characteristics and a short follow-up duration, which may not capture long-term outcomes and side effects.

Conclusion

GNSRS is an effective and safe second-line treatment option and should be planned for patients with primary TN who fail to respond to medical treatment. Following GNSRS treatment, significant reductions in pain intensity, as measured by the BNI pain scale, were observed.

In addition, the dosage of medications used for the treatment of TN is decreased after GNSRS.

Although the complications of GNSRS on short-term follow-up were minimal and transient, further studies are recommended to evaluate the long-term benefits and side effects of GNSRS in TN.

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Conflict of Interest

Authors declare no conflict of interest.

Data availability

Data are available upon reasonable request.

ORCID

Zaki Hasan 0000-0003-0585-7241
Bassam Arkawazi 0000-0001-7908-9869
Mohammed Albayati 0000-0001-6338-7087

References

[1] Rose FC. Trigeminal neuralgia. Archives of neurology, 1999, Sep 1;56(9):1163-4.

[2] Ameli NO. Avicenna and trigeminal neuralgia. J Neurol Sci 1965; 2: 105–7.

[3] MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain 2000.; pt 4):665–676. https://doi.org/10.1093/brain/123.4.665

[4] Koopman JS, Dieleman JP, Huygen FJ, de Mos M, Martin CG, Sturkenboom MC. Incidence of facial pain in the general population. PAIN®. 2009 Dec 15;147(1-3):122-7. https://doi.org/10.1016/j.pain.2009.08.023

[5] Fromm GH, Sessle BJ. Introduction and historical review . In: Fromm GH, Sessle B, eds. Trigeminal Neuralgia. Current Concepts Regarding Pathogenesis and Treatment. Boston: Butterworth-Heinemann, 1991; 1–26. https://doi.org/10.1001/archneur.1984.04050220102026

[6] Gorgulho AA, De Salles AA. Impact of radiosurgery on the surgical treatment of trigeminal neuralgia. Surg Neurol. 2006;66:350–356. https://doi.org/10.1016/j.surneu.2006.03.046

[7] Petit JH, Herman JM, Nagda S, DiBiase SJ, Chin LS. Radiosurgical treatment of trigeminal neuralgia: evaluating quality of life and treatment outcomes. Int J Radiat Oncol Biol Phys. 2003;56:1147–1153. https://doi.org/10.1016/s0360-3016(03)00264-5

[8] Hodaie M, Coello AF. Advances in the management of trigeminal neuralgia. Journal of neurosurgical sciences. 2013 Mar;57(1):13-21.

[9] Pollock BE. Surgical management of medically refractory trigeminal neuralgia. Curr Neurol Neurosci Rep. 2012;12:125–131. https://doi.org/10.1007/s11910-011-0242-7

[10] Little AS, Shetter AG, Shetter ME, Bay C, Rogers CL. Long-term pain response and quality of life in patients with typical trigeminal neuralgia treated with gamma knife stereotactic radiosurgery. Neurosurgery. 2008;63(5):915–923. discussion 923–924. https://doi.org/10.1227/01.neu.0000327689.05823.28

[11] Urgosik D, Liscak R, Novotny J, Jr, Vymazal J, Vladyka V. Treatment of essential trigeminal neuralgia with gamma knife surgery. J Neurosurg. 2005;102(suppl):29–33. https://doi.org/10.3171/jns.2005.102.s_supplement.0029

[12] Lopez BC, Hamlyn PJ, Zakrzewska JM. Stereotactic radiosurgery for primary trigeminal neuralgia: state of the evidence and recommendations for future reports. J Neurol Neurosurg Psychiatry. 2004;75(7):1019–1024. https://doi.org/10.1136%2Fjnnp.2003.018564

[13] Mathieu D, Effendi K, Blanchard J, Séguin M. Comparative study of gamma knife surgery and percutaneous retrogasserian glycerol rhizotomy for trigeminal neuralgia in patients with multiple sclerosis. J Neurosurg. 2012;117(suppl):175–180. https://doi.org/10.3171/2012.6.gks12987

[14] Bangash TH. Trigeminal Neuralgia: Frequency of Occurrence in Different Nerve Branches. Anesthesiology and Pain 2011; 1(2):70-72. https://doi.org/10.5812%2Fkowsar.22287523.2164

[15] De Toledo IP, Conti Réus J, Fernandes M, Porporatti AL, Peres MA, Takaschima A, et al. Prevalence of trigeminal neuralgia: A systematic review. J Am Dent Assoc 2016; 147(7):570-576.e2. https://doi.org/10.1016/j.adaj.2016.02.014

[16] Al-Quliti KW. Update on neuropathic pain treatment for trigeminal neuralgia. The pharmacological and surgical options. Neurosciences (Riyadh) 2015; 20(2):107-114. https://doi.org/10.17712/nsj.2015.2.20140501

[17] Al-Khafaji ZA, Ahmed MA. Efficacy of glycerol rhizotomy in trigeminal neuralgia: case series. AL-Qadisiya Medical Journal 2018; 14 (25): 9-17. https://doi.org/10.28922/qmj.2018.14.25.9-13

[18] Siqueira SR, Teixeira MJ, Siqueira JT. Clinical characteristics of patients with trigeminal neuralgia referred to neurosurgery. Eur J Dent 2009; 3(3):207-212.

[19] Siqueira SR, Nóbrega JC, Teixeira MJ, Siqueira JT. Masticatory problems after balloon compression for trigeminal neuralgia: a longitudinal study. J Oral Rehabil 2007; 34:88–96. https://doi.org/10.1111/j.1365-2842.2006.01680.x

[20] 20.Toda K. Side-to-side Asymmetry in Trigeminal Neuralgia: Multiple Factors Theory. Oral Science International 2009: 95-99. https://doi.org/10.1016/S1348-8643(09)80004-9

[21] Santo Neto H, Camilli JA, Marques MJ. Trigeminal neuralgia is caused by maxillary and mandibular nerve entrapment: greater incidence of right-sided facial symptoms is due to the foramen rotundum and foramen ovale being narrower on the right side of the cranium. Medical hypotheses. 2005 Jan 1;65(6):1179-82. https://doi.org/10.1016/j.mehy.2005.06.012

[22] Piagkou MN, Skandalakis P, Piagkos G, Demesticha T. Trigeminal pain and its distribution in different trigeminal nerve branches. Anesth Pain Med 2012; 1(4):271-272. https://doi.org/10.5812%2Faapm.3764

[23] Tuleasca C, Carron R, Resseguier N, Donnet A, Roussel P. Decreased Probability of Initial Pain Cessation in Classic Trigeminal Neuralgia Treated With Gamma Knife Surgery in Case of Previous Microvascular Decompression: A Prospective Series of 45 Patients With >1 Year of Follow-up. Neurosurgery 2015; 77 (1): 87-95. https://dx.doi.org/10.1227/NEU.0000000000000739

[24] Karam SD, Tai A, Wooster M, Rashi A, Chen R, Baig N, et al. Trigeminal neuralgia treatment outcomes following Gamma Knife radiosurgery with a minimum 3-year follow-up. J Radiat Oncol 2013; 3(2):125-130. https://doi.org/10.1007/s13566-013-0134-3

[25] Young B, Shivazad A, Kryscio RJ, St Clair W, Bush HM. Long-term outcome of high-dose γ knife surgery in treatment of trigeminal neuralgia. J Neurosurg 2013; 119(5):1166-1175. https://doi.org/10.3171/2013.1.jns12875

[26] Knafo H, Kenny B, Mathieu D. Trigeminal neuralgia: outcomes after gamma knife radiosurgery. Can J Neurol Sci 2009; 36(1):78-82. https://doi.org/10.1017/s0317167100006351

[27] Régis J, Tuleasca C, Resseguier N, Carron R, Donnet A, Yomo S, et al. The Very Long-Term Outcome of Radiosurgery for Classical Trigeminal Neuralgia. Stereotact Funct Neurosurg 2016; 94:24–32. https://doi.org/10.1159/000443529

[28] Faraj MK, Naji NA, Alazawy NM. The efficiency of the prescribed dose of the gamma knife for the treatment of trigeminal neuralgia. Interdisciplinary Neurosurgery 2018; 14: 9–13. https://doi.org/10.1016/j.inat.2018.05.017

[29] Tempel ZJ, Chivukula S, Monaco EA 3rd, Bowden G, Kano H, Niranjan A, Chang EF, et al. The results of a third Gamma Knife procedure for recurrent trigeminal neuralgia. J Neurosurg 2015; 122(1):169-179. https://doi.org/10.3171/2014.9.jns132779

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