The Efficacy of Gamma Knife® Radiosurgery Using Retrogasserian Approach in the Management of Trigeminal Neuralgia: A Prospective Study

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ABSTRACT:

BACKGROUND:

Tic douloureux is a debilitating disease presented as a recurrent unilateral short- living, electric, shock - like pain, abrupt in onset and termination, limited to the distribution of one or more division of trigeminal nerve.

OBJECTIVE:

To evaluate the effectiveness of Gamma Knife® radiosurgery (GKRS) using retrogasserian approach.

PATIENTS AND METHODS:

A follow up review was conducted on twenty patients who were treated with GKRS for refractory TN at our institution Dr. Saad Al-Witry Neuroscience Hospital in Baghdad, Iraq, between December 2019 and March 2021. T.N pain score was assessed using the Barrow Neurological Institute (BNI) Pain Scale. An ideal result was counted by post-GKRS BNI score of (I–III), whereas insufficiency outcome was (IV – V) of same scale.

RESULTS:

From the entire (twenty) GKRS procedures, (85%) of patients had result with remarkable relief in their complain (BNI I-III). No noteworthy relation was found between unacceptable outcome and age, sex, side of complain, period of symptoms. Only four cases (20%) developed undesirable outcome in form of facial numbness.

CONCLUSION:

Considering the satisfactory results in our own experience, GKRS is also offered as a feasible, effective, safe initial and repeat treatment modality targeting patients who were intractable to medical treatment.

KEYWORDS: Trigeminal neuralgia; Gamma Knife radiosurgery; Retrogasserian approach.

INTRODUCTION:

Trigeminal Neuralgia:

Trigeminal neuralgia (TGN), is a 5th cranial nerve disorder mostly presented with sporadic, excruciating, lancinating and electric like facial pain in one or more of three divisions (V-V3)[1]. It is usually provoked by movements or tactile stimulation of the face. Moreover, the bulk of facial pain in TN is unilateral (>95%). In general, it involves the maxillary (V2) or mandibular (V3) area of the face[2].

Some of the risk factors in developing TN are multiple sclerosis (MS), increased age, stroke, hypertension (in women), Charcot–Marie–Tooth disease, and tumours in the region of the trigeminal nerve root[3].

The pain associated with TN can be so severe and disabling causing profound psychological effects such as depression and anxiety.

A high-resolution neuroimaging is usually recommended to rule out other causes of facial pain[4].

The more anterior was the choice of target the lesser was the rate of complications, even with a maximal dose of 90 Gy. However, targeting the trigeminal nerve 5–8 mm away from the brainstem has been recommended in order to get an optimal response without significant trigeminal dysfunction[5].

The period to achieve good result after the GK has been found to be significant shorter in the retrogasserian method (mean 4.1 weeks) than in the dorsal REZ group (mean 6.4 weeks). Pain levels and symptom relief were standardized across patients using the BNI Pain Scale[5].

Mild facial paraesthesia was reported in around 17 % of cases, a disabling facial numbness (BNI IV) was recorded in 11.1 % of patients who were

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selected with retrogasserian method; nevertheless, these group had a positive result with BNI pain intensity score of I on follow - up. There were no reports of corneal numbness or dry eye syndrome cases[6]

PATIENT AND METHOD:

Patient Selection

A prospective study of twenty patients presented to Dr. Saad Al-Witry Neuroscience Hospital in Baghdad, Iraq during the period from December 2019 to March 2020 with TN were recruited in this study. General demographic characteristics including patients' age, gender, medical, surgical history, medication history, social and family history were collected. The frequency and the pain intensity scores were also analyzed in this study.

Inclusion criteria

- All patients with trigeminal neuralgia who were referred by neurologist to neuroscience hospital/ surgery department with pain refractory to medical therapy despite the maximum tolerated dose.
- All cases should have a BNI pain intensity score of IV or V.
- Only patients with primary Trigeminal neuralgia were recruited.

In order to rule out secondary causes for TN, in all cases an MRI imaging was done. Additionally, this imaging was also used to assess whether there is a neurovascular relationship. Pre-operative routine investigation was ordered for all cases who met the inclusion criteria. These involve a complete blood picture, renal profile, blood glucose level and viral screen**.**

Initial pain assessment

In this analysis, information regarding pain history were recorded using "The Barrow Neurological Institute Pain Intensity Score (BNI)" as primary assessment as well as a parameter for outcome. In order to record these, a questionnaire was designed to record patient's basic data, pain characteristics, BNI, and postoperative complication checklist.

Surgical technique

The procedure begins with fixation of the Leksell stereotactic frame to the patient's head whilst patient sitting upright facing forward and following administration of local anesthetic medications and inducing a conscious sedation. This is usually achieved by injecting a 2% lidocaine into four regions with one on either side of the forehead and two in the occipital area for screws placement. Once this is completed, the patient will then be moved to measurements room in which a special measurement helmet is placed on the frame to take measurements that are necessary for lesion targeting for the Leksell gamma knife software. Next step, patient was sent for CT brain and registration of patient information and ID number. Subsequently, images were transferred to the Gamma Knife computer workstation. Co-registration of CT with MRI of GAMMA protocol were done, Leksell Gamma Plan software was utilized to detect the radiosurgical target which is calculated as 7.5 mm from the dorsal root entry in retrogasserian approach (RG). A dose planning was performed by neurosurgeon. Dose planning for gamma knife surgery can accurately conform the isodose distribution to the target. In this study, a dose setting of 90 Gy was delivered to the 100% isodose in RG approach.

Consideration was taken to avoid delivering more than 15 Gy to the pons and brainstem at the maximal exposure point. To target the trigeminal nerve exactly at 7.5 mm distal to its exit from the pons, a single 4 mm beams was applied.

Follow-up protocol:

Following the primary assessment and GKRS procedure, patients were immediately examined for post-operative complications. Subsequently, three additional clinical visits at 1,6,12 months were arranged and cases were assessed using BNI. Additionally, continuation of trigeminal neuralgia pain control medication post GKRS were recoded. Initially, we carried out the follow-up assessment as face to face. However, due to the strict lockdown rules during COVID-19 pandemic, the final follow-up assessment at 12 months was performed as telephone consultation. Lastly, procedure failure was considered if post treatment BNI score of IV or V.

Ethical Issues:

Detailed written information about the GKRS, the risk and benefits were explained to the patients in order to obtain an informed written consent prior to the procedure. Additionally, patients were counselled regarding being included in this study and a verbal consent was taken.

RESULTS:

Age:

The mean age treated by gamma knife was 50.95 years, (range 34-68 years). The distribution of the age groups illustrated in Figure 1.

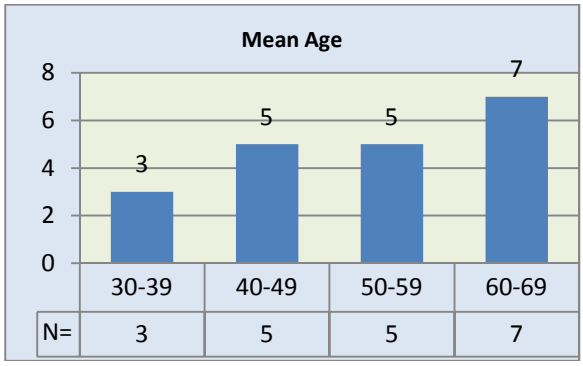

Figure 1:Age Distribution.

Gender: In this study, n=12 (60%) were females and n=8 (40%) were males with male to female ratio being illustrated in Figure 2.

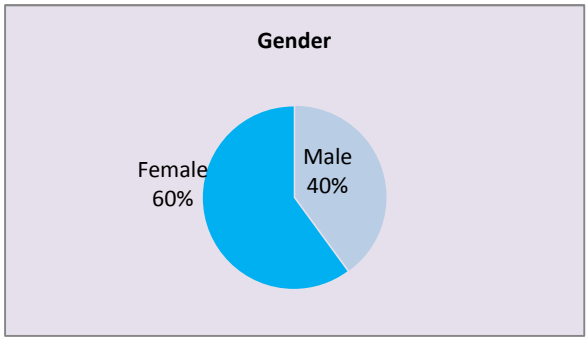

Figure 2:Gender Distribution

Details of Follow-Up Period
The median follow-up period was 13.5 months (range = 12-15).

Side of pain
Pain was on the right side in (15) (75%) whilst (5) (25%) were on the left side of the face as in Figure 3.

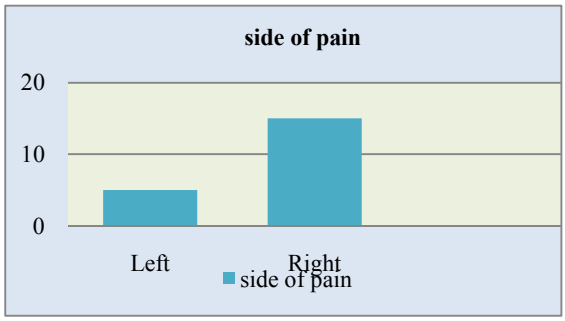

Figure 3: Side of pain.

Duration of medical management before Gamma knife:
Between 3 months to 10 years in most of the cases, illustrated in Figure 4.

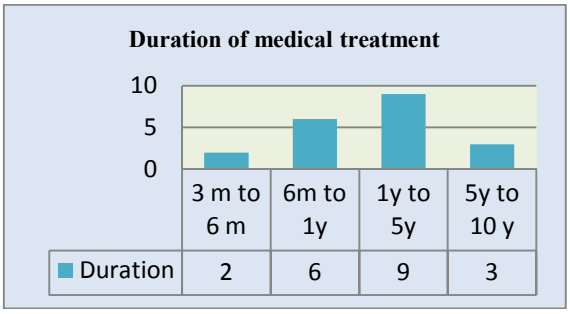

Figure 4: Duration of medical treatment.

Data Regarding Previous Treatments:
Gamma Knife radiosurgery was the first surgical procedure in (18) patients (90%). (10%) patients had prior surgical procedures and of these, (1) (5%) had only 1 previous intervention of GKRS, and (1) (5%) had previous MVD surgery.no previous history of injection or radiofrequency.

Probability of Freedom from Pain after Radiosurgery

Pain's severity was assessed using BNI scale as pre and post Gamma Knife with RG approach at the 12 months follow up.

A total of (17) patients (85%) became better in pain intensity after the Gamma Knife radiosurgical procedure with or without medication (BNI score I-III),

- 15% of patients have pain improvement to grade 2.
- 70%of patients have pain improvement to grade 3.
- 15%of them pain grade post gamma is 4.

Table 1: Pain intensity pre and post GKRS.

BNI	Prior to GKRS	After GKRS	p-value
1	0	0	1.0
2	0	3	0.072
3	0	14	<0.001
4	2	3	0.633
5	18	0	<0.001

*BNI: Barrow Neurological Institute
*GKRS: Gamma Knife Radio Surgery

Pain frequency per week PRIOR to Gamma Knife:
This study demonstrates the therapeutic efficacy of Gamma Knife in reducing pain frequency (Table 2&3). The mean weekly attacks were 21.5 at baseline, but 9.5 attacks per week after GKRS treatment.

Table 2: Pain frequency per week pre-GK.

Pain frequency per week	No. (%)
1-5	0 (0)
6-10	0 (0)
11-20	7 (35)
21-30	13 (65)

Pain frequency per week POST Gamma Knife:

Table 3: Pain frequency per week post GK.

Pain frequency per week	No. (%)
1-5	5 (25)
6-10	10 (50)
11-20	3 (15)
21-30	2 (10)

COVID-19 symptoms during recovery:

On the follow up assessment, one patient out of 20 cases reported worsening of pain intensity score (BNI IV-V). Interestingly, it was found that the patient has tested positive for COVID-19 during follow up period.

Prognosticators:

Analysis for previously published prognosticators of treatment failure is shown in Table 4. There was, however, no statistically significant difference between age, gender, laterality of pain, duration of symptom and treatment failure.

Table 4: Summary of some prognosticators and development of treatment failure (BNI IV–V).

Variable	Good outcome	Treatment failure	p-value
No. of patients	17 (85%)	3 (15%)	0.00001
Gender			
Male	6	2	0.1005
female	11	1	
Side of pain			
Rt	14	1	1.30002
Lt	3	2	
Age			
>60	5	2	0.2
<60	12	1	
Duration of symptom			
>12 months	11	1	0.3
<12 months	6	2	

Complications for Leksell frame application:

Only three patients developed an early complication after radiosurgery with pinhole site infection and treated with IV antibiotics. Overall, 4 out of 20 patients (20%) without previous facial sensory symptoms developed new sensory dysfunction later, such as paraesthesia or objective loss of facial sensation.

Table 5:Complications.

Complication	Facial numbness	Pinhole site infection
	4	3

Patient satisfaction:

A self-reported patient satisfaction questionnaire was collected at the follow up appointment. 17 out of 20 (85%) were pleased compared to (10%) of cases where the post-operative results did not meet their expectations.

Table 6: Patient satisfaction.

No regret	No opinion	I regret
17	1	2

DISCUSSION:

Achievement of Pain Relief:

Some authors have noted a latency interval to pain relief after radiosurgery of 1–2 months. In the present analysis, we found that (70%) of patients responded to treatment at a median of 1 month[7]. By 12 months after GKS, 15% of patients had not achieved maximum relief.

In our study, Pain relief was noted an average of (7-8) months after treatment. This time frame is consistent with previously published data[8].The best result, BNI Score I-II-III was achieved in 85% of patients. This report provides additional confirmation of the generally positive results reported by others[9,10].

Pain frequency:

The pain severity and attack frequency were significantly decreased on follow-up after GKRS. In our study, this technique reduced the mean pain frequency by more than a half. In Young *et al*. study the frequency of daily use of as-needed analgesia was largely decreased. The GKRS were enough to alleviate pain with 26.8% of patients showing excellent response with analgesia being no longer required[1]. However, in the majority of studies, changes in the frequency of attacks were not clearly described. A better understanding of this field requires more studies in the future. Our study adds supports for such area and provides data that may be useful for future trials.

Patient satisfaction:

With regards to patient satisfaction was reported to be high (85%), with the majority considering their treatment as successful and were happy they have undergone the procedure supporting evidence from a study done in 2015[11].

Complications

Our results of new-complain of facial numbness twenty percent is similar to a previously published study done by Riesenburger et al[8]. Our study failed to show any noticeable relation between known parameter such as age, sex, side of complain, period of symptoms and development of unfavorable result at last follow-up[12].

Previous procedure:

Given the low number of events in our series with only (2) patients having had undergone previous procedures (microvascular decompression and previous GK), that correlation could not be tested in our current study.

CONCLUSION:

Retrogasserian **GK** approach is a minimally invasive procedure to relief trigeminal neuralgia symptom. The significant symptom resolution prompt the discussion of using GK as the alternative first- or second surgical choice for TN. patient satisfaction was reported to be high with the majority considering their treatment as successful and were happy they have undergone the procedure.

REFERENCE:

1. Dhople AA, Adams JR, Maggio WW, Naqvi SA, Regine WF, Kwok Y. Long-term outcomes of Gamma Knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Journal of neurosurgery. 2009;111:351-58.
2. 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 ;65:1179-82.
3. Vasappa CK, Kapur S, Krovvidi H. Trigeminal neuralgia. BJA Educ. 2016;16:353–56.
4. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia Int J Headache. 2018;38:1–211.

5. Tavakol S, Jackanich A, Strickland BA, Marietta M, Ravina K, Yu C, Chang EL, Giannotta S, Zada G. Effectiveness of gamma knife radiosurgery in the treatment of refractory trigeminal neuralgia: a case series. Operative Neurosurgery. 2020;18:571-6.
6. Karam SD, Tai A, Wooster M, Rashid A, Chen R, Baig N, Jay A, Harter KW, Randolph-Jackson P, Omogbehin A, Aulisi EF. Trigeminal neuralgia treatment outcomes following Gamma Knife radiosurgery with a minimum 3-year follow-up. Journal of radiation oncology. 2014;3:125-30.
7. Dellaretti M, Reyns N, Touzet G, Sarrazin T, Dubois F, Lartigau E, et al. Clinical outcomes after Gamma Knife surgery for idiopathic trigeminal neuralgia: review of 76 consecutive cases. J Neurosurg. 2008;109 Suppl:173–78.
8. Riesenburger RI, Hwang SW, Schirmer CM, Zerris V, Wu JK, Mahn K, Klimo P, Mignano J, Thompson CJ, Yao KC. Outcomes following single-treatment Gamma Knife surgery for trigeminal neuralgia with a minimum 3-year follow-up. Journal of neurosurgery. 2010;112:766-71.
9. 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;63:915-24.
10. Little AS, Shetter AG, Shetter ME, Kakarla UK, Rogers CL. Salvage gamma knife stereotactic radiosurgery for surgically refractory trigeminal neuralgia. International Journal of Radiation Oncology* Biology* Physics. 2009;74:522-27.
11. Nanda A, Javalkar V, Zhang S, Ahmed O. Long term efficacy and patient satisfaction of microvascular decompression and gamma knife radiosurgery for trigeminal neuralgia. Journal of Clinical Neuroscience. 2015;22:818-22.
12. Mueller D, Obermann M, Yoon M-S, Poitz F, Hansen N, Slomke M-A, et al. Prevalence of trigeminal neuralgia and persistent idiopathic facial pain: a population-based study. Cephalalgia Int J Headache. 2011;31:1542–48.