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Original Article

Effectiveness of thalamotomy with Gamma Knife radiosurgery as a multitarget strategy in patients with complex trigeminal neuralgia

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ABSTRACT

Background: In the setting of refractory neuralgia or other complex facial pains, the intensity of the pain does not decrease despite medical and even surgical interventions. This report aims to describe the experience of an institution in the management of refractory trigeminal neuralgia and other complex facial pains with Gamma Knife radiosurgery (GKR), including thalamotomy as a multitarget strategy.

Methods: We conducted a retrospective observational study. Data were obtained from 50 patients with complex trigeminal neuralgia treated with GKR, in whom the thalamus was included as a target. The Visual Analog Scale (VAS) and the Barrow Neurological Institute (BNI) scale were considered before treatment and at the follow-up. The Wilcoxon test was used to compare the VAS scores and the McNemar test for the BNI scale.

Results: The mean age was 62.7 years (standard deviation = 16.3). The indications for management with thalamotomy were neuralgia refractory to medical management (68%), recurrent pain after previous rhizolysis with GKR (20%), atypical deafferentation-type pain in patients with radiofrequency background (10%), and anatomical deformation of the trigeminal nerve by a tumor (2%). Before treatment, all patients were classified as BNI V. At follow-up, a satisfactory response to treatment was described in 82.05% of cases ($P = 0.001$ McNemar). The median preoperative pain evaluated with VAS was 10 (interquartile range [IQR] = 10–10), while at follow-up, it was 6 (IQR = 1–7) ($P = 0.001$ Wilcoxon).

Conclusion: The thalamus is a versatile, effective, and safe therapeutic target for ablative management in patients with complex facial pain.

Keywords: Facial pain, Trigeminal neuralgia, Trigeminal nerve, Thalamotomy, Gamma Knife radiosurgery, Stereotactic radiosurgery

INTRODUCTION

Trigeminal neuralgia is a condition characterized by a high intensity and short-duration pain distributed in one or more divisions of the trigeminal nerve. It is recurrent with an abrupt onset and electrical nature. The symptom tends to be debilitating with a significant effect on the quality of life of the patients.[1]

Medical management with neuronal membrane-stabilizing drugs is the first-line treatment. The effectiveness in symptom control can be up to 90%; however, this effect may not be permanent and side effects can arise in up to 23% of cases, entailing the suspension of treatment in most of these cases.[2] When failures in medical treatment occur, interventional management is required. In some cases, the intensity of the pain does not decrease despite medical and even surgical interventions; these cases are considered refractory neuralgia. This condition implies a significant morbid burden not only derived from the direct cost of consultations to the emergency service but also from indirect costs related to work disability.[9]

Gamma Knife radiosurgery (GKR) allows a noninvasive treatment of the intracranial structures responsible for the conduction and interpretation of pain. In the setting of refractory neuralgia or other complex facial pains, its usefulness lies in the possibility of treating not only the trigeminal nerve as a unique target (rhizolysis) but also other structures, such as the thalamus. This report aims to describe an institution's experience in managing refractory trigeminal neuralgia and other complex facial pains with GKR, including thalamotomy as a multitarget strategy, analyzing its indications, results, and complications attributable to the treatment.

MATERIALS AND METHODS

We conducted a retrospective observational study. Data were collected from Fundación Clínica Shaio in Bogotá, Colombia. We obtained the approval of the Institution's Ethics Committee (DIB23-09). Data were obtained from 50 patients with complex trigeminal neuralgia treated with GKR, in whom the thalamus was included as a therapeutic target.

Pretreatment clinical variables, data from the radiation treatment, and follow-up data were collected from medical charts and phone interviews. For clinical outcomes, the Visual Analog Scale (VAS) and the Barrow Neurological Institute (BNI) scale were considered before treatment and at the follow-up time. Complications were described during the 1st-month posttreatment (acute complications) and in the last clinical control (chronic complications).

The data were analyzed using the statistical program STATA 17.0. For quantitative variables, normality in the distribution of the data was verified by graphs, the Shapiro-Wilk test, and kurtosis. According to the results, measures of central tendency were applied, mainly median with interquartile range (IQR) and mean with standard deviation (SD). For qualitative variables, proportions were calculated. The Wilcoxon test was used to compare the VAS scores and the McNemar test for the BNI scale. For this last scale, a satisfactory response was considered for BNI I, II, and III, and unsatisfactory for BNI IV and V. The cut-off point to establish statistical significance was 0.05 in both tests.

RESULTS

Fifty patients with refractory, secondary, or atypical trigeminal neuralgia in whom the thalamus was selected as a therapeutic target for ablative treatment through GKR were included. These patients were treated with Gamma Knife Perfexion between August 2015 and April 2022. 70% of the patients were women, while 30% were men. The mean age was 62.7 years (SD = 16.3). 38% of the patients had a background of previous surgical management (microvascular decompression), 24% of previous radiosurgery, and 48% of previous percutaneous management [Table 1].

The specific thalamic target selected for treatment with GKR was the central median nucleus of the thalamus, which we located having as the reference the intermediate point of the inter-commissural line, 10 mm posterior in the (y) axis, 10 mm lateral in the (x) axis, and 3.5 mm higher on the (z) axis [Figure 1]. The indications for the management with thalamotomy were neuralgia refractory to medical management (68%), recurrent pain after previous rhizolysis with GKR (20%), atypical deafferentation-type pain in patients with radiofrequency background (10%), and anatomical deformation of the trigeminal nerve by a tumor (2%). In patients with recurrent pain after first treatment with GKR, the median time to relapse was 9 months (IQR 2–13).

In 85% of the cases, treatment included the retrogasserian portion of the ipsilateral trigeminal nerve and the contralateral posteromedial thalamus (ipsilateral rhizolysis plus contralateral thalamotomy), being refractory neuralgia, and deafferentation-type pain, as the two main indications. In 10% of cases, the selected targets were the ipsilateral sphenopalatine ganglion and the posteromedial thalamus, mainly in patients with refractory pain and autonomic manifestations. In 5% of cases, the contralateral posteromedial thalamus was the only target when an anatomical deformation of the nerve was described. All procedures were performed in one session on an outpatient basis. The median time per fraction was 120 min (IQR 100–142). The median hospital stay was 4.4 h (IQR 3.7–5.8). Other treatment variables are described in Table 2.

Regarding follow-up, data from 39 patients were obtained with a mean follow-up of 38.5 months (SD = 19.1). Before treatment, all these patients were classified as BNI V. At follow-up, 10.2% were classified as BNI I, 5.1% as BNI II, 66.6% as BNI III, and 17.9% as BNI IV. Any case was classified as BNI V after treatment. A satisfactory response to treatment was described in 82.05% of cases ($P = 0.001$ McNemar). The

Table 1: Summary of the main pretreatment characteristics of the patient sample.

Pretreatment characteristics	*n*=50	%
Gender		
Female	35	70
Male	15	30
Interventional background		
Microvascular decompression	19	38
Gamma Knife radiosurgery	12	24
Percutaneous management	24	48
Radiofrequency gangliolysis	4	8
Gasser ganglion block	4	8
Sphenopalatine block	3	6
Peripheral facial block	1	2
Glycerol gangliolysis	1	2
Peripheral nerve electrical stimulation	1	2
Mechanical compression	1	2
Glycerol rhizolysis	1	2
Laterality		
Left	26	52
Right	24	48
Affected branch		
V1	25	50
V2	38	76
V3	29	58
Origin		
Primary	31	62
Neurovascular conflict	14	28
Secondary	19	38
Tumors of the cerebellopontine angle	7	14
Postherpetic	7	14
Multiple sclerosis	2	4
Posttraumatic	2	4
Ischemic	1	2
Selected target		
Thalamus	50	100
Trigeminal nerve	41	82
Sphenopalatine ganglion	5	10

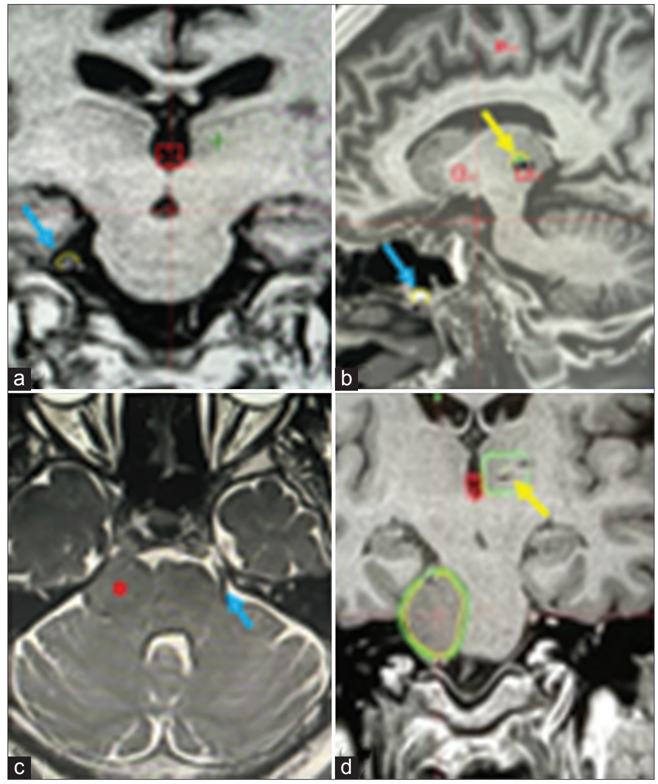

Figure 1: GKR treatment planning images. a) Coronal slide of T1-weighted MRI shows the prescription dose area of the right trigeminal nerve (63 Gy) (blue arrow) and the planning axis of the left thalamus (green cross) located lateral and superior to the posterior inter-commissural line (PC) (red box). b) Sagittal slide of the T1-weighted MRI shows the sphenopalatine ganglion prescription dose area (45 Gy) (blue arrow) and the thalamus prescription dose area (70 Gy) (yellow arrow). The anterior (red box - AC) and posterior (red box - PC) limits of the inter-commissural line can also be observed. c) Axial slide of heavily T2-weighted MRI shows a tumor in the right cerebellopontine angle (red asterisk) deforming the right trigeminal nerve, which is not observed, unlike the left trigeminal nerve (blue arrow). d) Coronal slide of T1-weighted MRI of the same patient in image c, shows the tumor of the right cerebellopontine angle (red asterisk), with the prescription dose of 12 Gy (yellow circle) and the safety dose of 10 Gy (green circle). The prescription dose of the thalamus (70 Gy) is shown in the yellow circle indicated by the yellow arrow and the green circle around it corresponds to the safety dose (10 Gy).

median preoperative pain evaluated with VAS was 10 (IQR 10–10), while at follow-up, it was 6 (IQR 1–7) (P = 0.001 Wilcoxon). The ablative effect was verified in magnetic resonance imaging 1 year after treatment [Figure 2].

Concerning acute complications, 74.3% of patients did not present any complications. 23% had a transient headache, 7.6% had pain at the frame's fixation points, and 2.5% had nausea. All manifestations responded satisfactorily to medical treatment. At the time of the last follow-up, there were no cases of painful anesthesia or corneal ulcers. Paraesthesias were the only complication described in 17.9% of patients.

DISCUSSION

Although the majority of cases of trigeminal neuralgia have a satisfactory response to medical treatment, there are some cases in which there is a failure of this treatment modality or the adverse effects force to consider interventional alternatives. Microvascular decompression is the most effective in symptom control, but it has a potential risk of complications such as infection, hemorrhages, fistula, and injury of nervous structures. Other options, such as radiofrequency, neurolysis with glycerol, or compression with a balloon, although less invasive, tend to have variable effectiveness and also have a potential risk of complications, with painful anesthesia as the most prominent.[3]

Table 2: Gamma Knife radiosurgery treatment data.

Target	Maximum dose (Gy)	Prescription dose (Gy)	Isodose (%)	Collimator (mm)	Shots (*n*)
Thalamus	130–140	65–70	50	4	1
Trigeminal nerve	90	63	70	4	1
Sphenopalatine ganglion	90	45	50	4	1

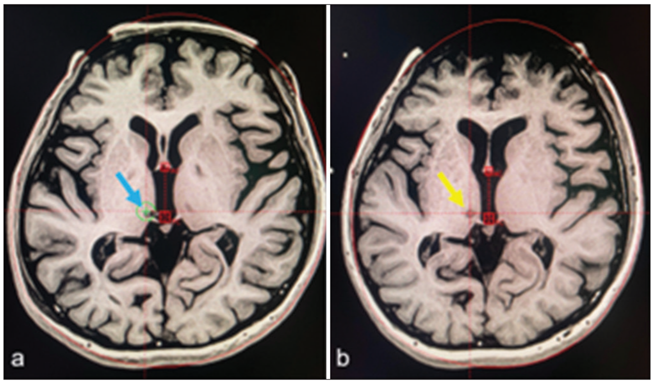

Figure 2: Ablative effect of GKR. (a) Sagittal slide of T1-weighted MRI planning radiation dose delivery to the right thalamus (blue arrow). (b) control image one year after treatment shows a hypointense area at the treatment site (yellow arrow) confirming the ablative effect at the level of the right posteromedial thalamus. The upper red box (AC) corresponds to the anterior limit of the inter-commissural line, and the lower red box (PC) to the posterior limit.

Stereotactic thalamotomy through thermal ablation radiofrequency has been used for the treatment of pain since shortly after the beginning of stereotaxy application.[5,11] Initially, the lateral-specific sensory thalamic nuclei were the therapeutic target due to their relationship with the interpretation of pain intensity; however, the occurrence of sensory disturbances and deafferentation pain caused this technique to fall into disuse.[8] Subsequent studies described that ablative treatment in the nucleus of the medial thalamus, more exactly in the posterior part of the thalamus and closer to the wall of the third ventricle[15], was more effective in reducing pain with fewer side effects.[4,16]

Ablative thalamotomy can be used for the management of different oncologic and nononcologic painful syndromes.[7] However, it has been described that medial thalamotomy is even more effective for the treatment of pain located in the upper part of the body. Franzini *et al.*,[6] and Lovo *et al.*[12] found that patients treated for facial deafferentation pain had better pain outcomes than those treated for other pain syndromes.

In this series of patients with complex facial pain, we emphasize not only the effectiveness of GKR in terms of reducing the intensity of facial pain but also the versatility of this method when selecting the therapeutic target depending on the clinical characteristics or the patient's needs. As it is noninvasive management that combines the principles of stereotaxy with ionizing radiation, we can consider multitarget management, including structures that participate in the transmission and interpretation of pain, such as the trigeminal nerve, thalamus, sphenopalatine ganglion, and even the cingulum.[13,14] In our study, we highlight how the thalamus can be an interesting therapeutic target not only in cases of neuralgia refractory to multiple treatments but also in cases where there are anatomical changes of the trigeminal nerve either due to atrophy secondary to previous treatment with radiation or deformation due to a lesion with mass effect.

Data reported in the literature suggest that thalamotomy with GKR can produce an initial pain reduction in 43.3–100% of the patients; however, in some cases, it fails to provide long-term pain control [7], whereby close monitoring of patients is important. In a systematic review, Franzini *et al.*,[7] described relief of facial pain in 38% of patients undergoing medial thalamotomy as the only target in the last follow-up. In addition, in the context of refractory neuralgia to multiple treatments, secondary or atypical facial pain, trigeminal neuropathy, or deafferentation-type pain, rhizolysis with GKR may not be as effective as typical neuralgia.[10] In our series, a satisfactory response was observed in 82% of patients with an average follow-up time of close to 3 years. This suggests that including the peripheral (nerve) and central (thalamus) components of pain may achieve better pain control than isolated targets.

Although the technique is considered safe with an estimated risk of complications of <5%, some reports have described complications attributable to radiation such as headache, nausea, vomiting, diplopia, contralateral weakness of upward gaze, vertigo, hemianesthesia, paresthesia, and progressive hemiparesis.[7,15] In our experience, most of the complications were transient (headache and nausea), with a satisfactory response to medical management. In the long term, although a not negligible number of cases with facial paresthesias occurred, these were mostly referred to as nondisabling, and there were no cases of painful anesthesia.

Limitations

Even though the most frequent and representative indication was refractory neuralgia, other indications were described and included in the final analysis. This can generate some grade of heterogeneity in the sample despite having as a common feature the ablative management in the thalamus.

CONCLUSION

The thalamus is a versatile, effective, and safe therapeutic target for ablative management in patients with complex facial pain. It can be part of a multitarget strategy adaptable together with other structures involved in the pain pathway, which can increase effectiveness compared to treatment with a single target.

Ethical approval

The Institutional Ethics Committee approval is obtained , No:DIB23-09.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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