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Current gamma knife treatment for ophthalmic branch of primary trigeminal neuralgia

Guo-Yong Shan[1], Hao-Fang Liang[2], Jian-Hua Zhang[3]

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[1]The Radiotherapy Department of Zhengzhou People's Hospital, Zhengzhou 450052, Henan Province, China
[2]Department of Medical Equipment Inspection, Zhengzhou 450003, Henan Province, China
[3]The Faculty of Biomedical Engineering of Zhengzhou University, Zhengzhou 450001, Henan Province, China
Correspondence to: Jian-Hua Zhang. The Faculty of Biomedical Engineering of Zhengzhou University, Zhengzhou 450001, Henan Province, China. petermails@zzu.edu.cn

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Abstract

• AIM: To probe into problems existing in gamma knife treatment of ophthalmic branch of primary trigeminal neuralgia (TN), and propose a safe and effective solution to the problem.

• METHODS: Through sorting the literature reporting gamma knife treatment of refractory TN in recent years, this article analyzed the advantages and problems of gamma knife treatment of primary TN, and proposed reasonable assessment for existing problems and the possible solution.

• RESULTS: Gamma knife treatment of TN has drawn increasing attention of clinicians due to its unique non-invasion, safety and effectiveness, but there are three related issues to be considered. The first one is the uncertainty of the optimal dose (70-90GY); the second one is the difference in radiotherapy target selection (using a single isocenter or two isocenters); and the third one is the big difference of recurrent pains (specific treatment methods need to be summarized and improved).

• CONCLUSION: For patients with refractory TN, gamma knife treatment can be selected when the medical treatment fails or drug side effects emerge. The analysis of a large number of TN patients receiving gamma knife treatment has shown that this is a safe and effective treatment method.

• KEYWORDS: Gamma knife; ophthalmic branch of trigeminal neuralgia; literature analysis
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INTRODUCTION

Trigeminal neuralgia (TN) is a common functional disease of nervous system[1], and it shows as repeatedly paroxysmal megalgia at trigeminal nerve distribution area, with the severe pain being unbearable, so it is commonly known as No.1 pain in the world. TN is commonly seen in clinical, but its cause is not very clear, and there are mainly the central nervous abnormal discharge, peripheral vascular compression and virus infection and other theories. The treatment mechanism of stereotactic radiosurgery (SRS) is to make the trigeminal nerve feel the root degeneration and then block the incoming pain through radiosurgery, thus to achieve the therapeutic purpose. As a stereotactic neurosurgical treatment method, the gamma knife treatment of TN has been clinically recognized[1-3].

Gamma knife treatment of TN has drawn increasing attention of clinicians with its unique non-invasion, safety and effectiveness, but there are still many related issues needing to be further studied, and its effectiveness and safety are to be further improved. This article anatomizes the problems in gamma knife treatment of refractory TN through analyzing the literature.

MATERIALS AND METHODS

Materials

Medical basis of ophthalmic branch of TN Mostly TN occurs to middle-aged population, and domestic statistics of its prevalence rate is 56 of 100,000 persons. The pain is mainly unilateral, more common at the right side. Ophthalmic branch of TN breaks out suddenly, often having a trigger point, and according to the typical outbreak features, it is not difficult for clinical diagnosis. TN is clinically divided into primary TN and secondary TN, and the latter means that the pain outbreak is caused by a specific organic disease, while the TN without clear causes and without positive signs of nervous system is primary. The treatment of secondary TN is mainly by removing the cause, but the treatment of primary TN is relatively difficult due to unknown causes[4]. At present, most scholars believe that the causes of primary TN may be associated with local vascular compression, virus infection, nerve degeneration, demyelination and other factors, and the main clinical

manifestation of primary TN is the pain of unknown causes. Long-term refractory pains make patients unbearable and overwhelmed with sorrow, and it seriously affects their lives, or even leads to dysfunction of the body, resulting in very serious consequences. Therefore, the mitigation and relief of the pain have become the necessary measures in clinical circumstances. The refractory TN with the failure of medical treatment or serious adverse drug reactions should be intervened with surgical means.

Reports about gamma knife treatment of TN The principle of gamma knife treatment of TN is not yet quite clear, and the dose of 75-95Gy is insufficient to cause necrosis of nerve fibers. It is usually considered that it is caused by high dose of irradiation damaging sensitive synapses and then nerve conduction block is produced, and this is consistent with the result. It is clinically observed that pains of the patients decrease or disappear after the treatment; generally feeling is not affected or patients have transient facial hypoesthesia. The continuous increase of irradiation dose cannot improve the efficacy, nor can it reduce the recurrence rate of TN patients. With the prolongation of clinical observation, the recurrence of TN is increasingly common, and the possible reason is that the factors causing damage to the trigeminal nerve are always there, and that neuroglia cells self-repair the synapses damaged by gamma-ray and re-establish connections. Indications of gamma knife are relatively wide, being non-invasive and safe, and its clinical application is increasing year by year, but the recurrence rate is 3%-15%, and there are still many issues which need further studies.

In recent years, with rapid development of imaging technology, computer technology and stereotactic technique, the stereotactic gamma knife radiosurgical treatment of primary refractory TN has achieved good efficacy, and has attracted high concerns of counterparts home and abroad. In fact, the application of gamma knife for treating TN already has a history of more than 50 years. In 1970s, the Swedish neurosurgical professor Lekse Ⅱ [5] was the first who used stereotactic radiosurgical technology treating two TN patients with X-ray irradiating the trigeminal ganglion, with the irradiation dose of 16GY and 22GY respectively, and the pains of two patients disappeared 1-5 months after the treatment. In 1995, Règis[6] irradiated the trigeminal ganglion with the 4mm or 8mm collimator with a dose of 35-75GY, and the effective rates were all about 50% . In 1996, Kondziolka[7] reported the results of 50 cases who underwent gamma knife treatment of TN, and all of them were positioned with MRI and the targets were the root entry zone (REZ) of the trigeminal nerve, using a single 4mm collimator with a center dose of 60-90GY, and the effective rate was 86%, with 6% of treatment failure and 6% of facial hypoesthesia. In 1998, Young [8] reported the results of 110 cases undergoing gamma knife treatment of TN, with MRI positioning and REZ as targets, and he used a single 4mm collimator with a center dose of 70-80GY, with an effective rate of 88% , 11.8% of treatment failure, 2.7% of facial hypoesthesia and 3.3% of pain recurrence. The reports in foreign literature in recent years show that the gamma knife treatment of TN is not only safe and effective, but also significantly improves the quality of life at the meantime of relieving pains [9-11]. China's stereotactic radiosurgery has developed in early 1990s, and with the gradual increase in cases of treatment, the experience on treatment becomes richer and richer, with the treatment outcomes being consistent with foreign reports[12-15].

Methods The international references that have reported on primary trigeminal neuralgia treatments in the past twenty years included more than forty articles at home and abroad. And retrospective investigation was conducted to analyze the factors of gamma knife treatment of TN.

At present, the statistics of gamma knife treatment of primary TN home and abroad has reached tens of thousands of cases, and from the first case of treatment till today, the researches of scholars in all countries have never ceased, aiming to continuously improve the cure rate and reduce the incidence of complications. The efficacy of early treated patients is poor, which may be related to positioning ways or target selection and the dose [16], and high-precision image data is the key to target selection.

For gamma knife treatment of TN, accurate positioning is the basis, and errors will be generated in installation of the first stock, MRI scanning, image transmission as well as image processing and treatment process. In the light of these factors, the focus is to analyze relevant issues in three aspects: (1) Individual difference of optimal dose selection; (2) Difference of irradiation target selection; (3) Analysis of various factors affecting pain recurrence. Therefore, this article analyzes issues about the above three aspects in domestic and foreign reports with the method of retrospective analysis.

RESULTS

Through nearly two decades of references, the retrospective investigation of the international 30 references obtained unanimous opinion about using gamma knife treatment of TN, reported home and abroad. On the one hand, the gamma knife is used for the unprogressive TN patients for whom drug therapies are ineffective or have side effects; on the other hand, it is a safe and effective treatment method with the gamma knife for the TN patients. The result analysis shows that the treatment of TN with stereotactic

radiosurgical technology has an effective rate of about 90%, about 10% of complications and about 10% of treatment failure. The 10% of treatment failure may be associated with the positioning accuracy, target selection and irradiation dose.

Individual Difference of Optimal Dose Selection The effect of pain relief is poor with too small dose of primary TN treatment; while overdose may damage the function of the nerve. Most scholars claim the dose selection of 70-90GY currently, but which one is the optimal dose remains unknown. It has been found from the completed comparative study on different doses that the largest dose of at least 70GY is more likely to fully relieve the pain than that of 60GY or 65GY. The effective rate does not improve significantly when the dose is up to above 90GY, but the likelihood of complications increased, and this has been confirmed in Kondziolka's experiment.

Difference of Irradiation Target Selection There is no final conclusion in respect of using a single isocenter or two isocenters for the nerve irradiation length. At present foreign countries mostly use a single 4mm collimator to irradiate, while domestic reports mostly use two 4mm collimators to expand the irradiation area to improve effective rate, and this has achieved good results [17,18]. The setting of a single target in the treatment often faces the dilemma between dose and efficacy. The setting of two targets not only makes the gamma-ray better consistent with trigeminal nerve root, but also expands the irradiation volume of the trigeminal nerve, making the nerve degeneration more thorough and complete, thus to make up for the insufficient irradiation of trigeminal nerve possibly caused by a single target. However, the treatment with two targets will also increase the incidence of complications in the meantime of expanding therapeutic area.

Difference of Pain Recurrence More and more follow-up results show that the efficacy is poor when the ganglion is selected as the irradiation target volume, and that pains are prone to recur, so this method has been discarded by the clinical. Selecting the REZ of the trigeminal nerve as the target volume of gamma knife treatment of TN has been recognized by stereotactic neurosurgery, as this section of nerve is easy to show in MRI [19, 20] without myelin wrapping, and it is a relatively sensitive area for radiotherapy. Comparatively big difference [21-23] of complications and pain recurrence show that the specific treatment method really needs to be summarized and improved. Besides, it is short of reports related to the long-term follow-up results of gamma knife treatment of TN, and the effective rate, complication rate and recurrence rate should be evaluated after long-term follow-up observation[24].

DISCUSSION

Gamma knife treatment of TN has drawn increasing attention of clinicians with its unique non-invasiveness, safety and efficiency, but there are still many related issues needing to be further studied, and its effectiveness and safety are to be further improved. Most scholars claim the dose selection of 70-90GY currently, but what is the optimal dose remains unknown. It has been found from the completed comparative study on different doses that the largest dose of at least 70GY is more likely to fully relieve the pain than that of 60GY or 65GY. The effective rate does not improve significantly when the dose is up to above 90GY, but the likelihood of complications increased, and this has been confirmed in Kondziolka's experiment. There is no final conclusion with regard to using a single isocenter or two isocenters for the nerve irradiation length. At present foreign countries mostly use a single 4mm collimator to irradiate, while domestic reports mostly use two 4mm collimators to expand the irradiation area to improve effective rate, and this has achieved good results. Currently, America is undergoing the experiment of comparing the irradiation effects of 1 isocenter and 2 isocenters as well as an experiment on trigeminal neurosurgical histology and ultrastructure, and domestic scholars also conduct the comparative analysis of gamma knife treatment of primary TN with two targets and a single target, and we look forward to new breakthroughs and more researches in this area[17]. According to reports on some recent treatment results, relatively big difference [21-23] of complications and pain recurrence shows that the specific treatment method really needs to be summarized and improved. Besides, it is short of reports related to the long-term follow-up results of gamma knife treatment of TN, and the effective rate, complication rate and recurrence rate should be evaluated after long-term follow-up observation[24].

For patients with refractory TN, gamma knife treatment can be selected when the medical treatment fails or drug side effects emerge. More and more TN patients receiving gamma knife treatment shows that this is a safe and effective treatment method. Many years of researches on the clinical application of stereotactic radiosurgical technology has proved that it is a treatment method with mature technology, accurate positioning, stable mechanical properties, small intracranial lesions, few pains, high effective rate and few complications. It now has been widely used in neurosurgical field worldwide and has become another reliable alternative in addition to the scalpel for neurosurgeons. The stereotactic radiosurgical technology of gamma knife will also play an increasingly great and amazing role with the development of social science and technology as well as the continuously deepening research on treatment.

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