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Mechanisms and Clinical Practice of Integrated Traditional and Western Medicine Treatment for Brain Gliomas

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Abstract:

Glioma is the most common malignant tumor in the central nervous system, which is difficult to treat and prone to recurrence. In recent years, traditional Chinese medicine (TCM) has shown unique advantages in reducing the toxicity of radiotherapy and chemotherapy and improving the quality of life of patients. However, the specific mechanism and systematic integration of integrated traditional Chinese and Western medicine (TCM and WM) treatment still need to be further explored. This article systematically reviews the progress of basic and clinical research on the treatment of glioma with TCM. The results show that some active components of TCM can inhibit the progression of glioma through mechanisms such as inducing tumor cell apoptosis and inhibiting DNA repair. Clinical observations indicate that the combination of TCM and WM can effectively alleviate bone marrow suppression caused by temozolomide chemotherapy, improve patients' cognitive function, and to some extent, prolong survival. This study provides theoretical support and practical basis for the integrated TCM and WM treatment of glioma. In the future, large-scale clinical research should be further carried out, the mechanism of action of TCM should be deeply explored, and the standardized and individualized application of integrated TCM and WM treatment should be promoted.

Keywords: Glioma; Integrated Traditional Chinese and Western Medicine; Toxicity Reduction; Tumor Microenvironment; Molecular Mechanisms.

1. Introduction

Brain gliomas are the most common primary malignant tumors of the central nervous system, accounting for approximately 80% of all intracranial malignant tumors [1]. Among these, glioblastoma multiforme (GBM) is the most aggressive neuroepithelial tumor, characterized pathologically by ab-

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normal proliferation of tumor cells and infiltrative growth along white matter fiber tracts, forming complex pathological interfaces with normal brain tissue. This unique biological behavior poses three core challenges in clinical treatment: surgical resection is often incomplete, conventional radiotherapy and chemotherapy frequently lead to drug resistance, and targeted therapy is limited by significant tumor heterogeneity.

Although modern diagnostic and therapeutic technologies have continued to improve in terms of surgical resection, radiotherapy and chemotherapy regimens, and targeted therapy, improvements in patient outcomes remain limited. The latest clinical data show that even with standardized treatment, the median survival time for GBM patients remains around 15.6 months, and the five-year relative survival rate for malignant brain tumor patients is only 35.7%, significantly lower than that for non-malignant brain tumor patients [2]. More concerning is that current treatment methods are associated with significant adverse reactions (such as bone marrow suppression and cognitive dysfunction) and heavy economic and psychological burdens on patients, severely impacting their quality of life. Therefore, exploring effective treatment modalities for brain gliomas is an urgent and important task.

In response to this treatment dilemma, the medical community is actively exploring multidisciplinary integrated treatment models. Against this backdrop, traditional Chinese medicine (TCM) continues to innovate and develop, demonstrating synergistic and complementary therapeutic value when combined with Western medicine. Unlike modern medicine‘s direct cell-killing strategies targeting tumor cells, TCM employs multi-targeted, multi-level mechanisms of action, demonstrating significant advantages in regulating the tumor microenvironment and enhancing the body‘s disease-resistance capabilities. Clinical studies on TCM-Western medicine combination therapy have yielded preliminary results in improving toxicity reactions from radiotherapy and chemotherapy, extending progression-free survival, and enhancing patients‘ quality of life. However, there is currently a lack of systematic summarization and organization in this research field. Therefore, this paper summarizes and organizes the intrinsic mechanisms of TCM regulation in the treatment of brain glioma, investigates the regulatory mechanisms of effective components of Chinese herbal medicine and their mediated signaling networks in the treatment of brain glioma, and explores the synergistic effects of integrated traditional Chinese and Western medicine (TCM and WM) treatment, with the aim of providing detailed information for further exploration of the molecular mechanisms of brain glioma and for integrated TCM and WM treatment.

2. Modern Medical Overview of Brain Glioma

Brain glioma is a tumor originating from glial cells and is the most common primary intracranial tumor. The 2021 edition of the World Health Organization Classification of Tumors of the Central Nervous System clearly divides gliomas into four grades: Grade 1 and Grade 2 are low-grade gliomas, while Grade 3 and Grade 4 are high-grade gliomas [3].

Currently, Western medicine‘s clinical treatment strategies for gliomas primarily include two main approaches: non-surgical treatment (chemotherapy, targeted therapy, immunotherapy) and surgical treatment. The clinical treatment process for this disease involves surgical resection, followed by temozolomide capsule chemotherapy combined with concurrent radiotherapy, and then six cycles of adjuvant chemotherapy to improve patient survival [4]. In recent years, the use of TCM syndrome differentiation treatment in conjunction with Western medicine for the treatment of brain gliomas has also gained increasing attention. During chemotherapy, the treatment principles may focus on tonifying qi and nourishing essence, transforming dampness, and harmonizing the stomach. Post-chemotherapy, the emphasis shifts to tonifying qi, resolving stasis, detoxifying, and dispersing nodules, with treatment tailored to the stage of the disease through syndrome differentiation.

3. Western Medical Treatment Strategies for Brain Glioma

3.1 Theoretical Foundation of Western Medical Treatment for Brain Glioma

The treatment system for glioma is based on the deep integration of molecular pathology and clinical techniques. The IDH gene, or isocitrate dehydrogenase, when mutated, significantly enhances the sensitivity of chemotherapy drugs through metabolic reprogramming. Meanwhile, the TNF receptor-associated factor 4 (TRAF4) and retinoblastoma protein-binding protein 4 (RBBP4) pathways expressed in grade 4 glioblastoma have been confirmed as the core mechanisms of drug resistance: TRAF4 maintains the activity of tumor stem cells, and RBBP4 accelerates damage repair. However, only when precise molecular diagnosis is combined with cutting-edge clinical techniques can theoretical advantages be translated into survival benefits for patients. Based on a deep understanding of the molecular characteristics of tumors, modern surgical techniques and comprehensive treatment strategies can be precisely implemented in a systematic manner. Surgical

advancements rely on precise positioning tools such as the neuro-navigation system to protect critical functional areas in real time, and fluorescence-guided technology marks tumor boundaries with an accuracy of 0.2 millimeters. Comprehensive treatment adopts a stepwise strategy: tumor treatment electric fields interfere with the cell division cycle of cancer cells and work synergistically with chemotherapy drugs; surgical resection creates an immune clearance window; intelligent nanoparticles [5,6] simultaneously achieve localization and drug delivery, precisely delivering drugs during the open period of the blood-brain barrier. This „resection-control-clearance“ three-stage model systematically builds a treatment closed loop based on the biological characteristics of tumors.

3.2 3.2 Western Medical Clinical Treatment of Glioma

Pediatric low-grade glioma (pLGG) and glioma usually have an indolent biological behavior, such as vision loss, epilepsy, endocrine dysfunction, motor disability, and poor quality of life. The treatment goal has shifted from merely pursuing survival rate to maximizing the long-term quality of life of patients. Under this treatment concept, chemotherapy remains the preferred first-line treatment for most recurrent or progressive pLGGs. Common chemotherapy regimens include ① carboplatin alone or in combination with vincristine (CV), ② thioguanine, procarbazine, CCNU, and vincristine (TPCV), and ③ vincristine alone. Although the progression-free survival (PFS) of carboplatin and vincristine may be slightly lower than that of TPCV (without statistical significance) [7], this combination avoids the risk of secondary malignancies and infertility. Therefore, given the indolent nature of pLGG, this combination is preferred to reduce long-term sequelae. Technological advancements offer the potential to limit normal brain exposure to low-dose radiation, and the chemotherapy treatment mode of multi-drug combination or single drug use provides a safer treatment option for pLGG in specific anatomical locations that are difficult to access surgically. The timing and selection of individualized tumor-directed interventions for different pLGG patients also reflect the current need in Western medicine clinical treatment of glioma to focus on functional outcomes rather than just survival.

4. Treatment Strategies for Brain Glioma Using TCM

4.1 Theoretical Basis and Syndrome Differentiation Approach of TCM in treating Glioma

TCM in treating glioma is guided by the core principles of „holistic concept“ and „syndrome differentiation and treatment“. This theory holds that the disease is located in the brain and is closely related to the dysfunction of the liver, spleen and kidney. Its pathogenesis is often caused by the interweaving of pathological factors such as wind, phlegm, blood stasis, toxins and deficiency. In clinical syndrome differentiation, it is mainly divided into two categories: „pathogenic excess“ and „deficiency of the root“. Pathogenic excess includes the accumulation of real pathogenic factors such as wind, phlegm, blood stasis and toxins, while deficiency of the root is mainly manifested as deficiency of both qi and blood and yin deficiency of the liver and kidney. The treatment emphasizes the complementary relationship between strengthening the body‘s resistance and eliminating pathogenic factors. For example, Banxia Tianma Baizhu Decoction is commonly used for the syndrome of internal obstruction by phlegm turbidity to resolve phlegm and disperse nodules, while Tongqiao Huoxue Decoction is selected for the syndrome of internal obstruction by blood stasis to promote blood circulation and unblock the meridians.

Research shows that the pathogenesis of glioma in TCM is complex, often presenting the characteristics of multiple pathological factors intertwined. Through the mechanism of multi-component and multi-target, TCM compound prescriptions play a comprehensive regulatory role in supporting the body‘s vital energy and eliminating pathogenic factors, demonstrating the unique thinking and advantages of integrated traditional TCM and WM in the treatment of glioma.

4.2 Clinical Treatment of Glioma with TCM Clinical Practice

For the dynamic evolution of glioma and the waxing and waning of the struggle between righteous and evil qi, TCM treatment should pay attention to the changes in the disease stage and comprehensively consider the patient‘s constitution. Due to the complex and variable etiological characteristics of this disease, in treatment, it is more necessary to clearly understand the pathogenesis and prescribe based on the severity and urgency of righteous deficiency and evil excess at different periods before and after surgery. In the clinical treatment example of Professor Xu Zhenye, a famous Shanghai TCM doctor, after the patient underwent left cerebral hemisphere lesion resection and stopped taking the oral chemotherapy drug temozolomide, occasional hand and foot twitching, right foot weakness, occasional dizziness, good appetite, regular bowel movements, and improved sleep were observed. The tongue was light red with a thin, greasy, and yellow coating. To achieve the goal of supporting the righteous qi, eliminating evil, benefiting qi, detoxifying, and resolving nodules,

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the prescription included earthworm and silkworm pupa to unblock the meridians and activate the collaterals, ligusticum and peach kernel to promote blood circulation and remove blood stasis, angelica to promote blood circulation and nourish blood, achyranthes bidentata to guide the drugs downward, lathyrus aphaca, snake six-grain, and gecko to detoxify and fight cancer, and malt and tangerine peel to strengthen the spleen, harmonize the stomach, and aid digestion. This case demonstrates that TCM can improve the quality of life and prolong the survival time of glioma patients, highlighting the advantages of TCM in treating glioma.

5. Clinical Practice of Integrated TCM and WM in the Treatment of Brain Glioma

The invasive and drug-resistant characteristics of brain gliomas significantly increase the difficulty of clinical treatment. Currently, modern integrated TCM and WM treatment for brain gliomas exhibits bidirectional regulatory features: at the molecular level, active components of TCM directly intervene in tumor cell proliferation and apoptosis through multi-target network regulation; at the clinical level, TCM formulations combined with conventional treatment produce synergistic antitumor effects while significantly reducing treatment-related toxic reactions.

5.1 Dual Regulation of Tumor Cell Proliferation and Apoptosis by Scutellaria baicalensis Extract

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In clinical use of TCM extracts, Scutellaria baicalensis affects the lung, liver, and In the clinical application of TCM extracts, Scutellaria barbata is attributed to the lung, liver and kidney meridians, and has the functions of clearing heat and detoxifying, promoting blood circulation to remove blood stasis, and diuresis to reduce swelling. Its extract, scutellarine B, has significant therapeutic effects on glioma in terms of anti-tumor, anti-inflammatory, antioxidant and immune enhancement. This component inhibits the proliferation of U251 cells through multiple mechanisms: on the one hand, it directly kills tumor cells by inducing DNA damage and apoptosis; on the other hand, it blocks DNA repair by inhibiting the expression of Rad51-mediated DNA repair proteins, thereby exacerbating genomic instability. In addition, the activation of the mitogen-activated protein kinase signaling pathway further enhances its inhibitory effect on glioma cell activity, fully demonstrating the multi-target intervention advantages of TCM extracts in clinical application.

5.2 The "Toxicity Reduction and Efficacy Enhancement" Effect of Integrated TCM and WM in the Treatment of Brain Glioma

Clinical practice of integrated TCM and WM in the treatment of glioma has demonstrated that TCM plays a dual role of enhancing efficacy and reducing toxicity throughout the entire intervention process. In terms of enhancing efficacy, TCM preparations (such as the combination of Hedyotis diffusa and Gentiana scabra) can increase the intratumoral concentration of chemotherapy drugs by regulating the permeability of the blood-brain barrier. Li et al.'s research, through XX method (which specific method is not provided), has revealed the principle (which active substances in TCM are effective and on what targets they act). Meanwhile, the latest research has confirmed that the combination of TCM and targeted drugs (such as MET inhibitors) can prolong the progression-free survival of some patients. This showcases the therapeutic value of the integration of TCM and Western medicine from the perspective of combining holistic regulation and targeted treatment [8,9]. In terms of reducing toxicity, Shenqi Fuzheng Injection can significantly reduce the incidence of grade 3-4 myelosuppression by 19.3% and improve cognitive function. The application of this preparation in the postoperative stage can also effectively alleviate myelosuppression induced by temozolomide. Additionally, the combination of acupuncture intervention (at acupoints such as Baihui and Fengchi) during radiotherapy and chemotherapy can further improve cognitive dysfunction [10]. Long-term survival data shows that Zhihe Powder combined with radiotherapy increases the 3-year survival rate to 61.3% (compared to 25.8% in the control group), and the use of phlegm-resolving and blood-stasis-removing prescriptions reduces the 2-year recurrence rate after surgery to 33.96% (compared to 56.0% in the control group) [11]. For postoperative complications, modified Zhenwu Decoction can effectively alleviate brain edema of the type characterized by yang deficiency and water retention, and reduce the reliance on diuretics [9]. These clinical evidences fully demonstrate the comprehensive advan-

tages of „reducing toxicity and enhancing efficacy“ in the integration of TCM and WM, providing a new strategy for individualized treatment of glioma.

6. Current Challenges and Future Directions

TCM has demonstrated unique multi-dimensional synergistic value in the comprehensive treatment of glioma. While modern medicine continuously improves therapeutic efficacy through surgical precision and radiotherapy technology innovation, TCM deeply participates in the remodeling of the tumor microenvironment by virtue of its multi-target regulatory advantages. Its active components, such as ginsenoside Rh2 and curcumin, can reverse the immunosuppressive state and improve the tumor immune microenvironment by promoting pro-inflammatory macrophage polarization and inhibiting myeloid-derived suppressor cell infiltration. Classic formulas like Shuangshen Sanjie Decoction can induce tumor cell death by regulating the expression of apoptosis-related proteins such as Bax/Bcl-2, and synergistically inhibit hypoxia-inducible factor and vascular endothelial growth factor signaling, thereby blocking tumor angiogenesis [12, 13]. To address treatment bottlenecks, nano-carriers modified with borneol and musk, as well as volatile oil from Acorus tatarinowii, significantly enhance the brain-targeted drug delivery efficiency and break through the blood-brain barrier limitations [13]. Clinical practice has confirmed that TCM intervention not only delays the progression of glioma but also exerts an integrated “synergistic effect and reduced toxicity” in improving radiotherapy and chemotherapy resistance, reducing side effects, and enhancing the quality of life of patients.

Additionally, future research on brain gliomas should be refined in the following areas: on one hand, further exploring the pathogenesis of brain gliomas, particularly the association between TCM syndromes and molecular biology; on the other hand, optimizing treatment regimens, such as combining TCM and Western medicine to improve clinical efficacy and reduce the incidence of adverse reactions.

7. Conclusion

This study systematically explored the mechanism and clinical value of integrated TCM and WM in the treatment of glioma. The results indicated that TCM exerts therapeutic effects through multiple mechanisms, including regulating the tumor microenvironment, inducing apoptosis, and inhibiting DNA repair. The integrated treatment approach demonstrated significant advantages in clinical application, effectively alleviating toxic and side effects such as bone marrow suppression and cognitive dysfunction caused by radiotherapy and chemotherapy, while also contributing to the extension of patient survival.

These findings offer new perspectives for addressing challenges such as drug resistance, toxic side effects, and tumor heterogeneity in glioma treatment. The systematic review of the integrated TCM and WM treatment model in this study provides a theoretical basis for further in-depth exploration and also offers a reference for formulating individualized treatment plans in clinical practice.

Current research still has certain limitations. Some mechanisms have not been fully clarified, and there is a lack of large-scale clinical data support. Future research should focus on in-depth exploration of the specific molecular mechanisms by which TCM regulates the tumor microenvironment, conduct high-quality clinical trials, promote the standardized application of integrated TCM and WM treatment, and ultimately improve the overall treatment effect of glioma.

Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

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