International Journal of Web of Multidisciplinary Studies
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
website: https://ijwos.com
Volume 3 Issue 5 , May 2026
E-ISSN : 3049-2424
DOI: https://doi.org/10.71366/ijwos

Pharmacotherapeutic Approaches in Glioblastoma: Pathophysiology and Role of Clinical Pharmacists in Optimizing Patient Care

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Article Info

Article History:

Published:31 May 2026

Publication Issue:
Volume 3, Issue 5
May-2026

Page Number:
748-757

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Abstract:

The most aggressive and prevalent primary malignant brain tumor in adults, glioblastoma is linked to poor overall survival, high recurrence rates, and quick progression. Glioblastoma's intricate pathophysiology includes aberrant cellular proliferation, angiogenesis, neuroinflammation, genetic abnormalities, and disruption of the blood–brain barrier, all of which support the growth of the tumor and its resistance to treatment. These pathological characteristics make illness management more difficult and severely restrict the efficacy of current therapeutic approaches. Temozolomide-based chemotherapy, corticosteroids, antiepileptic medications, targeted therapies, and novel immunotherapeutic agents are examples of current pharmacotherapeutic strategies. However, inadequate medication penetration into the central nervous system, tumor heterogeneity, chemoresistance, adverse drug responses, and drug-drug interactions related to multimodal therapy continue to result in unsatisfactory treatment outcomes. Through pharmacological therapy management, therapeutic drug monitoring, adverse drug response monitoring, drug interaction discovery, patient counseling, and supportive care interventions, clinical pharmacists contribute significantly to the optimization of glioblastoma management. Their involvement can enhance neuro-oncology patients' overall therapy results, medication safety, and treatment compliance. Furthermore, new therapeutic approaches like immunotherapy, precision medicine, molecular targeted therapy, and drug delivery systems based on nanotechnology may offer promise improvements in the treatment of glioblastoma. The pathophysiological processes of glioblastoma, contemporary pharmacotherapeutic strategies, and the growing involvement of clinical pharmacists in improving patient care and therapy outcomes are all highlighted in this study.

Keywords: Glioblastoma, Temozolomide, Neuroinflammation, neuro-oncology. clinical pharmacy

1. Introduction

Glioblastoma (GBM) is the most prevalent and malignant primary brain tumour in adults. Despite intensive therapeutic efforts, it is characterized by fast cellular proliferation and significant invasion into adjacent brain tissue, which contributes to its poor clinical outcome. Over the past few decades, increases in GBM patient survival have remained modest despite advancements in surgery, radiation, and chemotherapy [1]. It is responsible for almost half of gliomas and around 16% of primary brain tumors. GBM requires sophisticated therapeutic techniques and cutting-edge medical tools for diagnosis and treatment, just like other malignant brain tumors. Glioblastomas can develop as secondary tumors that develop from lower-grade astrocytomas, such as grade II astrocytoma or grade III anaplastic astrocytoma, or as primary (de novo) tumors that develop quickly without a precursor lesion. GBM has been divided into four main molecular subtypes based on genomic analyses using datasets produced by The Cancer Genome Atlas: proneural,

neural, classical, and mesenchymal. Each subtype has diverse gene expression patterns and behavioral traits, which contribute to variations in tumor behavior and responsiveness to treatment. The inability of therapeutic regimens to successfully penetrate the blood–brain barrier (BBB) and the emergence of drug resistance are two of the main obstacles in the management of GBM. Despite the widespread use of contemporary therapeutic methods, including as radiation, chemotherapy, and surgical resection, patient results are still poor, with a median survival span of roughly 14–15 months [2]. Glioblastoma treatment has advanced significantly over the last 20 years, especially with the use of tumor-treating fields, a non-invasive therapeutic technology that has shown clinical benefit in improving patient outcomes, and the introduction of Temozolomide (TMZ) chemotherapy. The extremely aggressive and invasive character of GBM still limits long-term survival despite these advancements, underscoring the critical need for more potent and creative therapeutic approaches to enhance both survival and quality of life. Bevacizumab, lomustine, and carmustine are further treatment alternatives that have demonstrated therapeutic value in the management of GBM. The PCV regimen, which combines procarbazine, lomustine, and vincristine to boost anticancer activity, is another frequently employed strategy [1, 3].

Glioblastoma's exceptional cellular heterogeneity contributes to its extreme resistance to the majority of anticancer treatments. In addition to differentiated glioblastoma cells, the tumor also contains glioma stem-like cells (GSCs) and other elements of the tumor microenvironment, such as endothelial cells, vascular pericytes, macrophages, and other immune cells. Tumor growth and treatment resistance are greatly influenced by this varied cellular makeup. By classifying GB into main molecular subtypes such proneural, classical, and mesenchymal, advances in transcriptional profiling and sequencing technology have further brought attention to the intricacy of GB. GSCs' dynamic nature and developmental flexibility add to this complexity. Because of their stem cell-like capacity for self-renewal and regeneration, which permits ongoing tumor development and recurrence, these cells are thought to be at the top of the tumor cell hierarchy. However, there are difficulties in accurately identifying and characterizing GSCs because they share a number of molecular markers with normal adult brain stem cells and progenitor cells [4].

New therapeutic approaches offer fresh promise for the treatment of glioblastoma despite these obstacles. To enable earlier identification and more accurate targeting of tumor cells, cutting-edge technologies aimed at enhancing the detection of cancer biomarkers are being investigated. To get over the restrictions imposed by the blood–brain barrier (BBB) and enable direct delivery of therapeutic drugs to the tumor site, innovative drug delivery systems—particularly those based on nanoparticles—are being developed concurrently. These novel strategies represent a hopeful development in the ongoing battle against GB since they may increase therapeutic efficacy, lower systemic toxicity, and improve overall clinical results. These advances also demonstrate the growing importance of pharmacists in the multidisciplinary care of GBM from the standpoint of clinical pharmacy. Chemotherapy regimen optimization, therapeutic response monitoring, drug-drug interaction identification, and treatment-related toxicities connected to medicines like temozolomide, bevacizumab, and other adjuvant therapies are all greatly aided by clinical pharmacists. In order to enhance quality of life, pharmacists are also involved in dose customization based on hepatic and renal function, medication adherence evaluation, supportive care management, and patient counselling [5]

2. Pathophysiology of Glioblastoma

Tumor Microenvironment

Tumor survival, progression, and resistance to treatment are all facilitated by the highly immunosuppressive and metabolically altered tumor microenvironment (TME) that glioblastoma creates. The polarization of macrophages toward the M2 phenotype, which inhibits T-cell activation and encourages immunological evasion by upregulating immune checkpoint molecules like PD-L1, is one significant mechanism. Poor treatment outcomes are a result of this compromised immune response, which permits tumor development to persist [6]. Extracellular acidity and hypoxia are other characteristics of the GBM microenvironment. Hypoxic circumstances trigger the activation of hypoxia-inducible factors (HIF1α and HIF2α), which improve DNA repair mechanisms, lessen radiation sensitivity, and promote glioma stem-like cell (GSC) maintenance. Proton and lactate transporters work in tandem with enhanced glycolysis and lactate generation to produce an acidic environment. Through ion trapping, this acidic TME decreases the efficacy of weak-base anticancer medications, increasing tumor invasiveness, stemness, and chemotherapy resistance.

GBM cells go through a metabolic reprogramming called as the Warburg effect, which causes energy production to switch from oxidative phosphorylation to glycolysis in order to survive in low-oxygen environments. Increased expression of glucose transporters and glycolytic enzymes such GLUT1, LDHA, PDK1, and HK2 supports this adaptation. Rapid tumor growth and defense against oxidative stress are further supported by altered lipid and nucleotide metabolism. Targeting metabolic pathways and glycolytic enzymes is being investigated as a potential tactic to enhance treatment response and overcome resistance in GBM as a result of these adaptations [7].

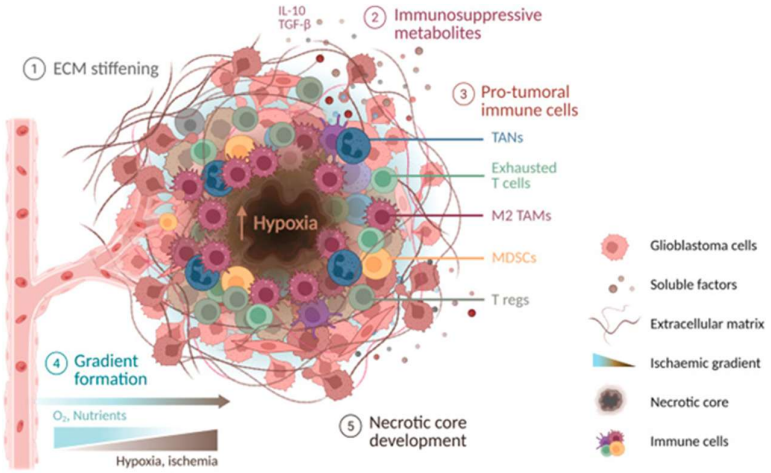

figure 1. [8].

Neuroinflammation

Glioblastoma has aggressive activity, fast progression, and a poor prognosis because to complex cellular and genetic abnormalities. Neuroinflammation, which is fueled by inflammatory mediators like interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α), is a significant part of the pathogenesis of GBM. A long-lasting pro-inflammatory feedback loop is created when these cytokines stimulate microglia and draw macrophages into the tumor microenvironment. This leads to the production of more cytokines and chemokines. Tumor development, invasion, and treatment resistance are all facilitated by this persistent inflammatory state. Because of the blood–brain barrier (BBB), which prevents viruses, poisons, and immune cells from entering through closely spaced endothelial cells, the central nervous system (CNS) was formerly thought to be an immunologically privileged region. Inflammatory activities in GBM compromise the BBB's integrity, making it more permeable and enabling more immune and inflammatory cells to infiltrate the brain tissue. In addition to creating a tumor-supportive milieu that encourages carcinogenesis, stromal support, tissue necrosis, and tumor survival, this BBB failure also contributes to chronic neuroinflammation. It's interesting to note that neuroinflammatory alterations have also been seen in areas of the brain that are far from the main tumor, such as the contralateral hemisphere. According to imaging research employing translocator protein positron emission tomography (TSPO-PET), contralateral neuroinflammation may be a useful indicator for forecasting the course of the disease and the prognosis of GBM patients [9, 10].

Invasion and Migration

Because glioblastoma cells adopt a variety of cellular, molecular, and metabolic adaptations to live, grow, and resist treatment, the disease is still very difficult to cure. GBM cells quickly adjust to adverse situations brought on by radiation, chemotherapy, hypoxia, and malnutrition. These tumors trigger a "angiogenic switch" to combat metabolic stress, which increases the expression of proangiogenic proteins like vascular endothelial growth factor (VEGF) and

causes new blood vessels to develop. The oxygen and nutrients needed for tumor development and invasion are supplied by this increased angiogenesis. Additionally, GBM cells experience molecular changes that encourage invasion and migration. Mesenchymal markers like N-cadherin and fibronectin are expressed more when pathways like PI3K/AKT are activated and the epithelial-to-mesenchymal transition (EMT) is induced. This increases the mobility and infiltrative ability of tumor cells. Furthermore, a subset of glioma stem cells (GSCs) plays a major role in both treatment resistance and tumor recurrence. These stem-like cells can self-renew, retain pluripotency, and regenerate tumors because they exhibit neural stem cell markers such CD133, Nestin, Musashi-1, and Bmi-1. Sonic Hedgehog (SHH), Notch, IL6/JAK/STAT3, and other signaling pathways are often dysregulated in GSCs and are linked to greater tumor grade and enhanced tumor aggressiveness. The capacity of GBM to avoid immune monitoring is another characteristic. By altering immune checkpoint pathways, GBM-associated endothelial cells produce an immunosuppressive tumor microenvironment. Immune checkpoint proteins like CD200 are overexpressed, which weakens antitumor immune responses by suppressing pro-inflammatory cytokines like IL-2 and IFN-γ. Additionally, GBM-derived substances including indoleamine 2,3-dioxygenase (IDO) and transforming growth factor-β (TGF-β) reduce antigen presentation and T-cell activation by impairing dendritic cell function. Together, these changes allow GBM cells to continue proliferating, evade immune detection, and remain resistant to traditional treatments [11].

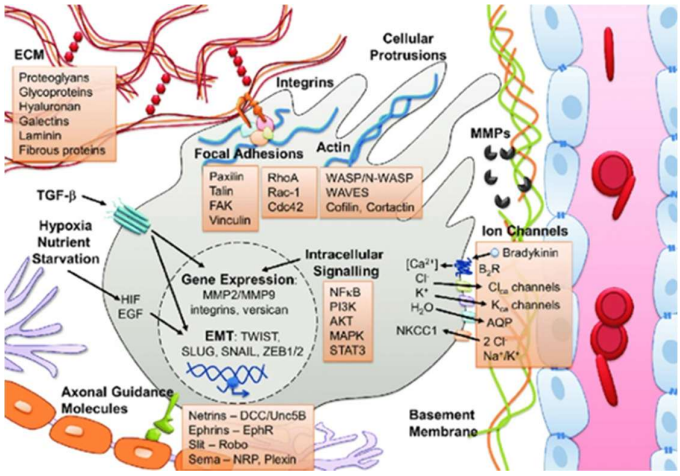

figure 2. [12]

Epigenetics

The formation of glioblastoma is significantly impacted by both genetic abnormalities and epigenetic changes that promote tumor growth, heterogeneity, and resistance to treatment. A key factor in the pathophysiology of GBM is epigenetic dysregulation, which modifies gene expression without altering the underlying DNA sequence. DNA methylation, histone changes, chromatin remodeling, and microRNA regulation are the main epigenetic processes at play. These changes can activate oncogenes, mute tumor suppressor genes, and encourage the survival and growth of tumors. DNA methyltransferases mediate DNA methylation, which frequently takes place at CpG islands close to gene promoter regions. Hypermethylation can affect tumor behavior and inhibit gene expression. Methylation of the O6-methylguanine-DNA methyltransferase (MGMT) promoter is one of the most clinically significant biomarkers in GBM. It is linked to better response to Temozolomide therapy and is a crucial prognostic and predictive marker. Determining the ideal threshold for MGMT methylation status is still difficult, though. Methylation, acetylation, and phosphorylation are examples of histone changes that control chromatin structure and gene accessibility. Dysregulation of histone-modifying enzymes, including histone deacetylases and histone methyltransferases, has been

implicated in gliomagenesis and tumor progression. Furthermore, by modifying nucleosome placement, chromatin-remodeling complexes (CRCs) control vital physiological processes as gene transcription, DNA repair, and cell-cycle regulation. Chromatin organization can be disrupted by mutations affecting CRC components, leading to aberrant gene expression patterns and accelerated tumor growth. These results point to epigenetic regulators as potential therapeutic targets for GBM treatment approaches in the future [6, 12].

3. Current Treatment Approaches

Since tumor recurrence and medication resistance continue to be significant clinical difficulties, glioblastoma treatment currently offers only modest improvements in survival. While surgery, radiation, and chemotherapy remain the cornerstones of standard care, breakthroughs in GBM therapeutics have given rise to a number of novel treatment modalities. These include noninvasive techniques like tumor-treating fields (TTF), immunotherapeutic approaches like immune checkpoint inhibitors (ICIs) and chimeric antigen receptor T-cell (CAR-T) therapy, and targeted treatments like epidermal growth factor receptor (EGFR) inhibitors. Despite these developments, GBM's high degree of invasiveness, wide genetic heterogeneity, and potent ability to evade treatment and the immune system make effective clinical management of the tumor challenging. These traits ultimately contribute to the advancement and recurrence of the disease by allowing tumor cells to withstand both established and novel treatments. In order to enhance long-term survival and quality of life in GBM patients, it is imperative that more accurate, tailored, and successful therapeutic approaches be developed [13].

Temozolomide (TMZ)

One frequently observed first-line alkylating chemotherapeutic drug used to treat glioblastoma is temozolomide (TMZ). While TMZ was synthesized in the 1970s and received clinical approval in the early 2000s, alkylating agents were first identified for their antitumor activity in the 1940s. TMZ can successfully pass through the blood–brain barrier (BBB) because of its lipophilic imidazotetrazine structure. Over half of GBM patients show resistance to TMZ therapy, despite its widespread use. The DNA repair enzyme O6-methylguanine-DNA methyltransferase (MGMT), which eliminates alkyl groups from the O6-guanine position and undoes TMZ-induced DNA damage, is a key mechanism behind this resistance. Because methylated MGMT decreases DNA repair activity and increases responsiveness to TMZ, MGMT promoter methylation is therefore regarded as a significant predictive biomarker. Mutations in the isocitrate dehydrogenase genes (IDH1 and IDH2), which are linked to a better prognosis and changed epigenetic regulation, are additional molecular factors affecting TMZ efficacy. Additionally, by fixing alkylated DNA lesions prior to apoptosis, DNA mismatch repair and base excision repair pathways may lessen the efficacy of TMZ. Treatment response is also strongly impacted by tumor suppressor p53 status [14]. TMZ resistance in GBM is further influenced by a number of dysregulated signaling pathways. In order to counteract the cytotoxic effects of TMZ, activation of the PI3K/AKT pathway encourages tumor cell survival, proliferation, angiogenesis, and inhibition of apoptosis. [15].

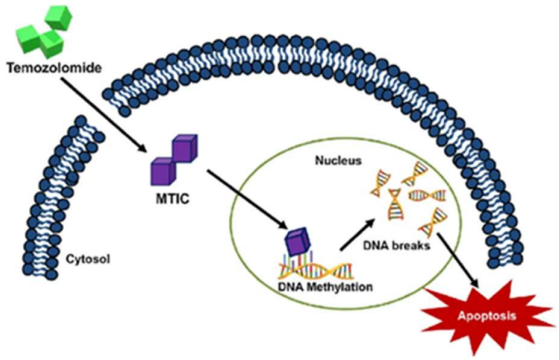

figure 3. [16]

Targeted Therapies

Numerous signaling pathways that support tumor growth, survival, invasion, and angiogenesis are abnormally activated in glioblastoma. Uncontrolled cellular proliferation, migration, differentiation, and resistance to apoptosis are all facilitated by the overexpression, amplification, or mutation of growth factor receptors, such as platelet-derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor (VEGFR), and epidermal growth factor receptor (EGFR). The aggressive character of GBM is largely due to these molecular abnormalities. Because of this, research on targeted therapies that block growth factor receptor signaling and tumor angiogenesis has grown in importance for the treatment of GBM. Small-molecule tyrosine kinase inhibitors (TKIs) and monoclonal antibodies against EGFR and VEGFR are examples of current therapeutic approaches; many of these have been assessed in phase II clinical trials. Inhibitors of PDGFR, integrins, and mammalian target of rapamycin (mTOR), which are all involved in cell signaling and tumor progression, are among the other targeted agents being studied. Despite these developments, tumor heterogeneity, adaptive resistance mechanisms, and the challenge of identifying the most effective molecular targets limit the clinical efficacy of targeted therapy in GBM. As a result, current research is concentrated on finding new therapeutic targets and creating individualized treatment plans that can enhance GBM patients' chances of survival [17].

Tumor Treating Fields (TTFields)

Glioblastoma treatment has improved with and the development of tumor-treating fields (TTFields), a novel and non-invasive therapeutic approach that disrupts mitosis and inhibits tumour cell proliferation. In comparison to patients receiving standard therapy alone, clinical studies have shown that patients receiving TTField therapy had better survival outcomes. Patients treated with TTFields had a median overall survival of roughly 22.6 months, while those who did not receive the therapy had a median overall survival of 17.4 months. Additionally, studies have demonstrated a median overall survival of approximately 20.9 months when TTFields and Temozolomide (TMZ) are combined, compared to nearly 15 months when standard therapy is used alone. The favorable safety and tolerability profile of TTField therapy is a significant benefit. Compared to traditional chemotherapeutic methods, the majority of patients tolerate the treatment well and experience comparatively few systemic side effects. In order to maximize therapeutic outcomes and enhance the quality of life for GBM patients, pharmacists are crucial in-patient education, adherence monitoring, supportive care needs management, and evaluation of combined therapy regimens involving TTFields and TMZ [14, 18].

Surgical Resection

Surgical resection is frequently used in the management of glioblastoma because research indicates that the safe removal of malignant glioma tissue is linked to better survival rates. Magnetic resonance imaging (MRI) is frequently used to determine the location of tumors, evaluate the severity of diseases, and direct surgical planning. Because it doesn't use ionizing radiation like computed tomography (CT) and offers better soft tissue visualization, magnetic resonance imaging (MRI) is especially useful for evaluating brain tumors. Maximal safe resection, which aims to remove as much tumor tissue as possible while maintaining neurological function and minimizing symptoms, is the main goal of surgery. However, because high-grade gliomas often occur close to important functional regions of the brain and infiltrate surrounding brain parenchyma, total removal is frequently difficult. Fluorescent-guided surgical resection has become a significant advancement in the treatment of GBM by increasing surgical precision. 5-Aminolevulinic acid (5-ALA), which selectively accumulates in glioma cells and fluoresces under particular wavelengths, is frequently used in this technique to help surgeons distinguish between malignant and healthy brain tissue during surgery. Compared to standard white-light surgery, fluorescent-guided resection has been linked to slower tumor progression and can detect infiltrative tumor regions that may not be clearly visible on conventional MRI [14, 19, 20].

4. Pharmacotherapeutic Challenges in Glioblastoma

Blood–Brain Barrier (BBB) and Blood–Brain Tumor Barrier (BBTB)

The BBB, which prevents the majority of therapeutic agents from entering the brain, limits the treatment options for glioblastoma. Drug delivery to all tumor regions is still insufficient in GBM, despite BBB disruption creating a modified blood–brain tumor barrier (BBTB). VEGF-driven angiogenesis contributes to uneven drug penetration and further modifies vascular structure [3].

Novel Drug Delivery Strategies

Convection-enhanced delivery (CED) and nanoparticle-based drug delivery are two strategies being researched to get around BBB-related restrictions. In experimental models, nanoparticles containing siRNA, targeted therapies, or immunotherapeutic agents have demonstrated increased survival. CED uses pressure-driven infusion to improve local intracranial drug distribution. Certain treatments, like immune checkpoint inhibitors and bevacizumab, may have therapeutic effects without actually entering tumor cells [3].

Immunosuppressive Tumor Microenvironment (TME)

Antitumor immunity is weakened by the highly immunosuppressive microenvironment that GBM produces. Natural killer (NK) cell function is compromised, T-cell activity is suppressed, regulatory T-cell populations are increased, and immune tolerance is encouraged by the tumor. Immunosuppressive cytokines like TGF-β and IL-10 are released by tumor-associated macrophages (TAMs) and microglia, which promote tumor growth and immune evasion [25].

Immune Checkpoint Dysregulation

GBM shows elevated expression of inhibitory signaling pathways like STAT3 and FasL as well as immune checkpoint molecules like PD-L1, IDO, and TIM3. These mechanisms limit the efficacy of immunotherapy by promoting T-cell apoptosis and suppressing immune surveillance [3].

Genetic Heterogeneity and Molecular Subtypes

Based on molecular signatures, GBM is divided into proneural, mesenchymal, and classical subtypes and exhibits significant genetic heterogeneity. Certain mutations affect immune cell infiltration, checkpoint receptor expression, prognosis, and possible response to immunotherapy. These mutations include PDGFRA, NF1, EGFR, PTEN, and IDH changes [3].

5. Role of Clinical Pharmacists

Dedicated neuro-oncology clinical pharmacists are rare, according to survey data from global neuro-oncology providers. Only about 29% of providers with pharmacist access in busy ambulatory clinics had a pharmacist dedicated exclusively to neuro-oncology, and only about two-thirds of these pharmacists had direct patient interaction. Developing practice guidelines, reviewing medications, and adjusting chemotherapy dosages were the main tasks; these were primarily "behind the scenes" rather than patient-facing.

Chemotherapy Management

For patients with glioblastoma, clinical pharmacists are essential to the optimization of chemotherapy regimens. Calculating and modifying dosages, scheduling treatment cycles, confirming chemotherapy procedures, and guaranteeing the safe administration of oral anticancer medications like temozolomide are among their duties. In order to reduce the risk of myelosuppression and other treatment-related toxicities, pharmacists also keep an eye on

hematological parameters, such as platelet counts and absolute neutrophil counts. Pharmacists also assist with the dosage and monitoring of bevacizumab therapy in cases of recurrent GBM. This involves keeping an eye on blood pressure, proteinuria, thromboembolic events, wound-healing issues, and bleeding indicators. Pharmacists help maximize treatment efficacy while lowering side effects and enhancing patient safety through ongoing therapeutic monitoring and cooperation with oncologists [21].

Management of Sequelae and Concomitant Medications

Due to treatment-related side effects and disease-related complications, GBM patients often need multiple supportive medications. The proper administration of corticosteroids, anticoagulants, antidepressants, antiemetics, antiepileptic medications, and other supportive therapies is supervised by clinical pharmacists. Pharmacists are crucial in identifying and preventing clinically significant drug-drug interactions, overlapping toxicities, and medication-related complications because these patients are frequently exposed to polypharmacy [22].

Patient and Caregiver Education

Patient counseling is an important part of clinical pharmacy care because many Glioblastoma patients have cognitive impairment, memory problems, exhaustion, and emotional distress. Regarding the administration of medications, dosage schedules, side effects, infection prevention measures, and adherence techniques, pharmacists give repeated verbal and written instructions. Involving caregivers is particularly crucial because they frequently help patients manage their medications and keep an eye out for any complications. In addition to addressing issues with quality of life and supportive care, pharmacists assist patients and caregivers in setting reasonable expectations for treatment results and disease progression. Pharmacists enhance treatment compliance, reduce avoidable medication errors, and enable patients and families to take an active role in the management of GBM through ongoing education and communication [21].

International surveys show that most busy neuro-oncology clinics lack a dedicated clinical pharmacist, and only about one-third of those with access have a pharmacist fully focused on neuro-oncology. Even when present, pharmacist roles are often indirect (medication review, dosing, guideline development) with limited direct patient contact.

Impact on Workflow, Cost, and Patient Care

A pilot study embedding a pharmacist in a neuro-oncology clinic documented 338 interventions in 147 encounters, mostly high complexity, including interaction checks, new therapy review, and advanced interventions. Reallocating these tasks from physicians to a 0.5 FTE dedicated pharmacist matched the existing medication-management workload and was cost-neutral or cost-saving, while freeing physician time for direct patient care. Other reports cite improved clinical efficiency, useful patient information, and reduced treatment-related stress when pharmacists are integrated into the team [23, 24].

By overseeing intricate chemotherapy and supportive regimens, avoiding interactions, and educating patients and caregivers, clinical pharmacists can play a crucial part in the treatment of glioblastoma. Pharmacists are underutilized in neuro-oncology, according to current data, but when they are integrated, they increase clinic productivity, encourage safer medication use, and probably improve patient satisfaction and overall care quality.

6. Conclusion

One of the most aggressive and challenging primary brain tumors, glioblastoma poses a number of pharmacotherapeutic difficulties that have a substantial impact on patient outcomes. The efficacy of currently available treatment options is diminished by factors like tumor heterogeneity, chemoresistance, frequent recurrence, severe adverse drug reactions, and limited drug penetration through the blood–brain barrier. Temozolomide, corticosteroids, antiepileptic medications, targeted therapies, and immunotherapy are examples of standard therapies that have limited survival benefits and are frequently linked to toxicity and drug interaction complications. Therefore, a multidisciplinary and customized therapeutic approach is necessary for the effective management of glioblastoma. Through medication therapy management, therapeutic drug monitoring, drug interaction detection and prevention,

adverse drug reaction monitoring, patient counseling, and supportive care management, clinical pharmacists are crucial to the optimization of pharmacotherapy. Their involvement can support better clinical outcomes and quality of life, increase patient safety, and improve medication adherence. Despite current limitations, emerging therapeutic strategies such as nanotechnology-based drug delivery systems, molecular targeted therapies, immunotherapy, gene therapy, and precision medicine show promising potential in overcoming existing treatment barriers. Continued research and collaborative neuro-oncology care are essential for improving the effectiveness of glioblastoma management and advancing future therapeutic outcomes.

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