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The impact of cognitive behavioral therapy on disease uncertainty, stressful life events, quality of life, anxiety, and depression in glioma patients undergoing chemotherapy: a quasi-experimental study

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Abstract

Objective To investigate the effect of cognitive behavioral therapy on disease uncertainty and stressful life events in glioma patients undergoing chemotherapy.

Methods This quasi-experimental study enrolled 90 glioma patients from Sanmenxia Central Hospital between January and December 2021. Patients were divided into an intervention group ($n=45$) or a control group ($n=45$). The intervention group received cognitive behavioral therapy provided by nurses, while the control group received routine nursing care. Pre- and post-intervention assessments were conducted using the Mishel uncertainty in illness scale (MUIS), life events scale (LES), self-rating anxiety scale (SAS), self-rating depression scale (SDS), and quality of life scale (WHOQOL-BREF).

Results After four cycles of chemotherapy, the study group demonstrated a statistically significant decrease in MUIS and LES scores compared to the control group ($p<0.05$). The study group showed significantly lower SAS and SDS scores than the control group ($p<0.05$). Finally, the study group reported significantly higher WHOQOL-BREF scores than the control group ($p<0.05$).

Conclusion The study revealed that the group that received CBT showed significant improvements in the psychological well-being of glioma patients undergoing chemotherapy. These findings suggest that incorporating CBT into standard nursing care can effectively improve the psychological well-being and quality of life of glioma patients during chemotherapy.

Keywords Cognitive behavioral therapy (CBT), Glioma, Chemotherapy, Disease uncertainty, Stressful life events, Quality of life, Anxiety, Depression

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Introduction

Glioma is a tumor that originates from glial cells in the brain and is a highly aggressive type of cancer with a poor prognosis. This type of tumor accounts for 50–60% of intracranial tumors, and its five-year survival rate is only 35–50% [1–3]. Additionally, the average survival time for these patients is often less than two years [4]. Common symptoms include increased intracranial pressure, seizures, neurological deficits, and cognitive impairments. Potential risk factors include exposure to high-dose ionizing radiation, rare genetic mutations, and potential environmental factors such as nitrite-rich foods or viral/bacterial infections [5].

Patients with diffuse glioma represent a distinct group within the cancer population, characterized by continuous tumor growth and ultimately inevitable death. Throughout the disease trajectory, patients experience a range of symptoms such as fatigue, cognitive impairment, and neurological deficits, leading to a high symptom burden and reduced health-related quality of life (HRQOL) [6–8], currently, surgery, radiotherapy, and chemotherapy are widely used for glioma treatment, among which radiotherapy and chemotherapy can effectively increase patient survival times and improve their quality of life. However, patients experience significant psychological distress and physical discomfort during the course of radiotherapy and chemotherapy. Most patients face varying degrees of anxiety and depression, which affect their adherence to the recommended treatments [9]. After a glioma diagnosis, many patients experience symptoms of depression. In fact, systematic reviews and longitudinal studies indicate that about 15 to 20 percent of glioma patients will experience depressive disorders within the first eight months following diagnosis [10]. Patients typically suffer from significant physical and psychological discomfort during treatment [11–13]. Chemotherapy side effects, such as fatigue, nausea, and hair loss, can lead to anxiety, depression, and decreased quality of life [14, 15]. Glioblastoma patients experience several radical challenges in their lives related to the uncertainty of their future and physical, psychological, and social changes [2]. Additionally, the uncertain nature of the disease and the long-term treatment process can further exacerbate these challenges.

Glioma not only causes physical pain and suffering but also triggers significant psychological distress. The invasive nature of surgery and the side effects of chemotherapy can lead to a range of negative emotions. These emotional responses can further exacerbate the disease's impact, affecting appetite, motivation, and overall quality of life. Gonzalez et al. found that the suppression of negative emotions is an important factor in tumor development [16]. One of the methods that is currently used alongside medical treatments is Cognitive Behavioral Therapy (CBT). This therapeutic approach is derived from the combination of cognitive and behavioral strategies [17]. Cognitive-behavioral therapy is a psychotherapy intervention that can help patients manage these negative emotions [18]. Cognitive behavioral therapy has been widely used to address the psychological needs of cancer patients.

The results of a study by Boele et al. in 2018, which examined the effectiveness of online psychological therapy in glioma patients, indicated that no evidence was found for the effectiveness of guided online self-help in terms of depression or health-related quality of life (HRQOL) in glioma patients [10]. The study by Zhao et al. (2021), which investigated the effects of comprehensive care based on cognitive-behavioral principles on the psychological functioning of glioma patients, showed that after the intervention, the FoP-Q-SF, SAS, SDS, and cancer-related fatigue scores in the intervention group were significantly lower than in the control group, while the quality of life scores in the intervention group were significantly higher than those in the control group [9].

Cognitive Behavioral Therapy (CBT) has emerged as a promising non-pharmacological intervention to mitigate these psychological burdens by helping patients develop effective coping mechanisms. However, limited studies have investigated its specific impact on disease uncertainty and stressful life events in glioma patients undergoing chemotherapy. This study aims to bridge this knowledge gap by evaluating the effectiveness of CBT in improving the psychological resilience and overall well-being of glioma patients, providing valuable insights for integrating psychological support into standard oncological care.

Materials and methods

Study design and setting

This study was designed as a quasi-experimental trial due to logistical constraints in conducting a fully randomized controlled trial at the Sanmenxia Central Hospital, China. A total of 90 patients diagnosed with glioma were enrolled. The participants were randomly divided into two groups: the study group received cognitive behavioral therapy (CBT), while the control group received standard nursing care.

Sampling and participants

Power analysis calculations with G*Power software indicate that (power = 80%, $p = 0.05$, number of groups = 2, and number of measurements = 2) 84 participants would be needed to detect an effect size of 0.55. Totally, 95 samples were assessed for eligibility, of which, 90 eligible participants allocated to the two

groups. Finally, all 90 participants finished the study (Fig. 1). This study employs a quasi-experimental design due to the non-randomized allocation of participants into different intervention and control groups. To minimize potential confounders, baseline characteristics of patients were analyzed and compared across groups, ensuring no significant differences in demographics or clinical features ($p > 0.05$). Inclusion criteria were patients with histologically or cytologically confirmed glioma diagnosis who received chemotherapy for the first time, those with anxiety score and depression score were in normal range, those with elementary education or higher, those who were willing to participate in follow-up interventions (telephone and video at home), those who were able to use electronic devices (mobile phone, iPad, Mp3), confirmed absence of cognitive-behavioral disorders and informed consent. Exclusion criteria were severe mental disorders, severe hearing impairment, severe medical conditions (heart, liver, kidney), use of sedative or anxiolytic/depressive drugs, age above 68, worsening condition during the intervention, and participation in other clinical trials or refusal to participate in this research. For glioma patients undergoing chemotherapy, the typical treatment cycle lasts around one month (28 days) [19]. In this study, we completed the questionnaires again after four cycles (4 months). The study purpose, procedures, and voluntary nature of participation were explained before obtaining informed consent.

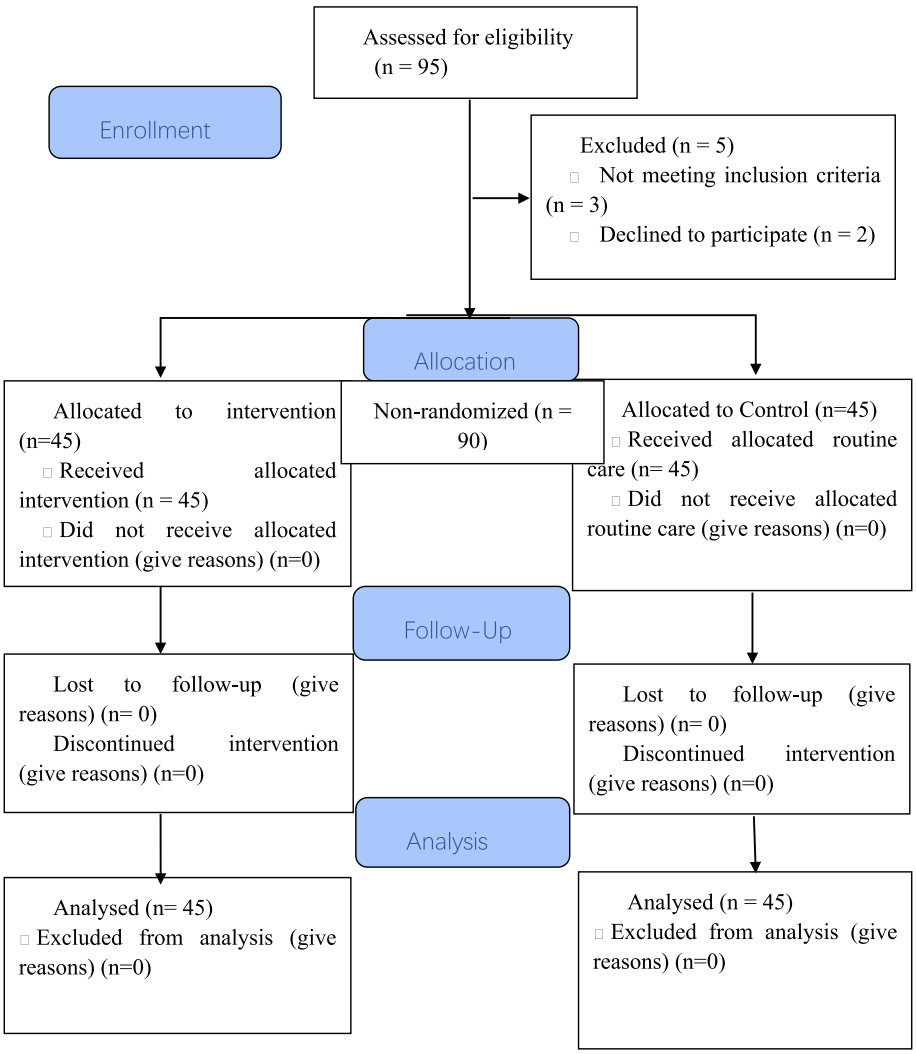

Fig. 1 The flow chart of the study

Measures

1- The Mishel Uncertainty in Illness Scale (MUIS) is a 32-item questionnaire designed to assess the level of uncertainty experienced by patients with chronic illnesses, including cancer [20]. Each item is rated on a 5-point Likert scale, with higher scores indicating greater uncertainty. The reliability and validity of the MUIS have been well-established in numerous studies. Cronbach's alpha coefficients have consistently ranged from 0.74 to 0.92, indicating strong internal consistency. Factor analysis has confirmed the tool's construct validity, demonstrating its ability to measure various dimensions of uncertainty in illness [21]. In this study, the MUIS was administered before and after four cycles of chemotherapy to assess changes in patients' perceived uncertainty. The Chinese version of the MUIS has been used in several studies to assess patients with chronic illnesses, including systemic lupus erythematosus. Its reliability has been established with a Cronbach's alpha coefficient of 0.865 and its construct validity was confirmed through factor analysis. This tool has been widely used in Chinese studies related to cancer and heart diseases [22].

2- The Life Events Scale (LES), developed by Yang and Zhang (1993), is a well-established tool for measuring the impact of life events in Chinese research. Its reliability and validity have been supported by Cronbach's alpha and factor analysis, respectively. The scale assesses three domains: family life (28 items), work/study (13 items), and social/other aspects (7 items). Each item is rated on a 5-point scale, with higher scores indicating greater stress. In this study, the LES was used to measure the impact of life events on glioma patients before and after four cycles of chemotherapy.

3- The Self-Rating Anxiety Scale (SAS) is a 20-item self-report measure used to assess anxiety symptoms. A higher score indicates greater anxiety, with scores above 50 considered clinically significant [23].

Sylvia Ramirez and James Lukenbill analyzed the psychometric properties of the SAS-ID, an adaptation of Zung's scale designed for adults with intellectual disabilities, developed by Lindsay and Mickie (1988). The SAS-ID was administered to 136 adults with intellectual disabilities and 96 caregivers. The scale demonstrated strong internal consistency reliability, with a coefficient of 0.80. It also showed moderate to strong correlations with other established measures of anxiety, including the Fear Survey for Adults with Mental Retardation ($r=0.40$), the PIMRA Anxiety Subscale ($r=0.44$), and the Taylor Manifest Anxiety Scale ($r=0.30$). Additionally, Zung's study found a strong correlation between self-administered and clinic-administered versions of the SAS test, with an overall correlation of 0.66 and a correlation of 0.74 for psychiatric patients [24].

4- The Self-Rating Depression Scale (SDS), developed by William W.K. Zung (1965), is a commonly used tool to measure depression. It consists of 20 questions that assess mood and physical symptoms. Respondents rate each item on a 4-point scale, with higher scores indicating greater depression. A score of 25–49 is considered normal, 50–59 is considered mild depression, 60–69 is considered moderate depression, and 70 or above is considered severe depression [25].

5- The WHOQOL-BREF, a shortened version of the World Health Organization Quality of Life questionnaire, has been widely used to assess quality of life across different populations, including in China. Previous research has demonstrated its reliability and validity in Chinese populations, particularly among medical students where Cronbach's alpha coefficients ranged from 0.711 to 0.794 for different domains (physical health, psychological health, social relations, and environment). The study also confirmed the construct validity through factor analysis, revealing that the four-domain structure fit the data well [26]. Each item is rated on a scale from light to heavy, with three items requiring reverse scoring [27]. The domain score is calculated as the mean score of the domain multiplied by four. A higher domain score indicates a better quality of life in the corresponding field. To investigate the impact of chemotherapy on quality of life, this study aimed to measure the WHOQOL-BREF scores of patients before and after four cycles of chemotherapy.

Intervention and data collection

The control group received standard nursing care, which included admission guidance, health education, treatment and nursing as prescribed by the doctor, keeping a clean and quiet ward environment, providing individualized dietary and nutritional guidance, explaining glioma chemotherapy-related knowledge and follow-up treatment plans, monitoring chemotherapy-related toxicities and side effects, and providing timely intervention, and delivering basic and psychological nursing care to prevent complications. All patients in the control group underwent four cycles of chemotherapy. For glioma patients undergoing chemotherapy, the typical treatment cycle lasts around one month (28 days) [19]. In this study,

we completed the questionnaires again after four cycles (4 months). The intervention lasted for four months, aligning with the duration of chemotherapy cycles. This study implemented a structured CBT framework based on traditional cognitive-behavioral therapy.

The study participants received cognitive behavioral therapy.

1 Cognitive therapy included the following:

A) Identifying and reconstructing negative thinking: Patients were educated about glioma chemotherapy, including disease knowledge and potential adverse reactions. The negative effects of anxiety and depression were explained. Discussions were held to address specific concerns and correct misunderstandings. Finally, the corresponding goals were set.
B) Identifying and challenging negative thoughts: Nurses familiarized patients with the ward environment and facilities, answered their questions promptly, and built trust. Through face-to-face communication, nurses assessed patients' negative psychology, thinking patterns, and subjective well-being. Also conducted structured cognitive assessments through interviews and self-report scales to identify negative thoughts. Common themes included fear of treatment failure, uncertainty about prognosis, and self-blame.
C) Breaking the vicious cycle: Regular group sessions were held to discuss disease-related knowledge and appropriate symptom management, encouraging patient engagement and positive mindset development. Health education manual of glioma chemotherapy was distributed to reinforce correct theoretical understanding, break the vicious cycle of negative thinking, and establish a positive cognitive framework.
D) Consolidating theoretical knowledge: Patients were guided to adopt new thought patterns, challenge negative thoughts, and employ positive thinking in problem solving through cognitive restructuring. This technique involves identifying negative thoughts, examining evidence that supports or refutes these thoughts, and replacing them with more realistic thoughts [28].

2 Behavioral therapy: Diaphragmatic breathing and breathing control exercises are used as part of CBT to reduce anxiety symptoms and regulate emotions. These techniques help decrease physiological responses to stress and are applied in the treatment of PTSD, anxiety, and depression. In CBT, breathing techniques are typically incorporated as part of relaxation and stress management strategies [29].

Patients were trained in abdominal breathing techniques, which involved the following steps:

A) Deep, slow inhalation: Patients were instructed to inhale deeply through the nose, allowing their abdomen to expand.
B) Breath holding: After inhaling, patients held their breath for one second.
C) Slow exhalation: Patients exhaled slowly through the nose or mouth, retracting their abdomen. This exhalation phase should last for 3–5 s.
D) Breath holding: After exhaling, patients held their breath for one second.
E) Repeat: Patients were encouraged to repeat this breathing cycle 10–15 times per session, 2–3 times per day.

For those with good physical fitness, the breath-holding duration could be increased, and the breathing pace could be slowed down. For those with poor physical fitness, the focus was on ensuring adequate inhalation without excessive breath holding. Abdominal breathing could be practiced in various postures, including sitting, lying down, walking, and running. The goal was to perform 100–150 abdominal bulges and retractions per session, continuing until slight fatigue or sweating was experienced. If accidental exhalation occurred during breath-holding, patients were advised to slowly swallow to prevent discomfort. This breathing training was implemented throughout the four cycles of chemotherapy.

Statistical analysis

The data in this study were analyzed using SPSS24.0. Data visualizations were created with Graphpad Prism 8.0. Measurement data with a normal distribution were expressed as mean ± standard deviation. Paired sample t-test was used for within-group comparisons, while independent sample t-test was used for between-group comparisons. Data that did not follow a normal distribution were presented as median (lower quartile to upper quartile). Categorical data were analyzed using Fisher's exact test. Statistical significance was determined at the $p < 0.05$ level.

Ethical consideration

The study was approved by the Ethics Committee of Sanmenxia Central Hospital. Informed consent was obtained from all participants, who were assured of the confidentiality of their data and were given the right to withdraw from the study at any time without any consequences.

Participants in the control group were provided with the opportunity to attend CBT sessions post-study, ensuring equitable access to psychological support.

Results

This quasi-experimental study was conducted at the Sanmenxia Central Hospital, China from January to December 2021. The study group consisted of 20 men and 25 women aged 29 to 67 years (49.48 ± 4.16). The control group included 22 males and 23 females aged 28 to 68 years old (49.15 ± 4.33) (Table 1).

There was no significant difference in the MUIS score between the two groups before the intervention. However, after four cycles of chemotherapy, the study group exhibited a statistically lower MUIS score than the control group ($p < 0.05$).

Before the intervention, there was no significant difference in SAS and SDS scores between the two groups ($p > 0.05$). However, after four cycles of chemotherapy, the study group exhibited a significantly lower SAS and SDS scores than the control group ($p < 0.05$).

Before the intervention, there was no significant difference in the LES scale scores between the two groups ($p > 0.05$). However, after four cycles of chemotherapy, the study group showed a significantly lower LES score than the control group ($p < 0.05$).

Before the intervention, there was no significant difference in the scores of WHOQOL-BREF between the two groups ($p > 0.05$). However, after four chemotherapy cycles, the study group reported a significantly higher WHOQOL-BREF score than the control group ($p < 0.05$) (Table 2 and Fig. 2).

Discussion

Glioma, the most common primary intracranial tumor, is characterized by high mortality and an unclear etiology. It accounts for 50% to 60% of intracranial tumors and originates from glial cells. Despite advancements in treatment, the 5-year survival rate remains limited at 35–50%, indicating a poor prognosis. Current treatment strategies primarily involve maximal safe surgical resection followed by radiotherapy and chemotherapy [30]. While chemotherapy can effectively prolong the survival time of glioma patients, it often induces numerous adverse effects, including neurocognitive impairments, psychological distress such as anxiety and depression, fatigue, and sleep disorders. These factors affect the quality of life of glioma patients undergoing chemotherapy [31]. Among these factors, emotional function has emerged as a critical determinant of the quality of life in glioma patients.

Zeng Xiaoqin found that negative emotions not only affect the quality of life for glioma patients undergoing chemotherapy but also correlate with cognitive impairment such as memory deficits. This underscores the significant adverse effect of negative emotions on patient outcomes [32]. These patients frequently exhibit symptoms of anxiety, depression, and low resilience [33]. These psychological challenges may be attributed to various factors, including low cognitive function, stressful life events, sudden lifestyle changes during early chemotherapy, and treatment-related side effects.

Traditional nursing practices have proven insufficient to address the complex needs of glioma patients undergoing chemotherapy. The conventional model, which relies heavily on medical staff instructions and specialist-ordered nursing care, often neglects patients' cognitive and psychological well-being. This can significantly impact treatment outcomes, leading to increased disease uncertainty and poor treatment adherence. To mitigate these challenges, healthcare providers must prioritize the psychological health of glioma patients and adopt innovative nursing models. These models should be designed to enhance cognitive function, alleviate negative emotions, and reduce stress associated with life-altering events [34–36]. Cognitive psychology principles suggest that maladaptive thoughts and beliefs can lead to a vicious cycle of negative emotions and behaviors [37]. Therefore, cognitive behavioral therapy offers a promising approach to address these issues. Liang Xiaoli et al. demonstrated the efficacy of CBT in alleviating chemotherapy-induced nausea and vomiting [38]. Therefore, this study aimed to investigate the effect of cognitive behavioral therapy on disease uncertainty and stressful life events in glioma patients undergoing chemotherapy. Negative emotions such as anxiety and uncertainty are key factors influencing treatment adherence and quality of life in glioma patients. Addressing these emotions through CBT can mitigate their impact and improve psychological well-being.

The results of this study showed that cognitive behavioral therapy improved patient outcomes compared to routine nursing care. Patients in the CBT group exhibited lower MUIS, SAS, SDS, and LES scores. Conversely, they reported higher scores on the WHOQOL-BREF scale. CBT aligns with a patient-centered approach, emphasizing the importance of

Table 1 Demographic characteristics of participants

Features	Control group ($n = 45$)	Intervention group ($n = 45$))	*P* value
Age (mean ± SD)	49.15 ± 4.33	49.48 ± 4.16	> 0.05
Gender (male/female)	(22/23)	(20/25)	> 0.05

Table 2 Study outcomes before and after four cycles of chemotherapy

Scale	Group	Before (Mean ± SD)	After (Mean ± SD)	t value	*P* value
MUIS Scale Score	Control	65.28 ± 4.44	41.15 ± 3.27	29.355	< 0.001
	Intervention	65.31 ± 4.37	36.19 ± 2.04	40.504	< 0.001
	t value	0.032	8.633		
	Effect size	0.007	1.819		
	P value	0.974	< 0.001		
SAS Scale Score	Control	68.12 ± 6.39	57.29 ± 4.15	9.535	< 0.001
	Intervention	68.14 ± 6.27	51.25 ± 3.14	16.158	< 0.001
	t value	0.015	7.786		
	Effect size	0.003	1.641		
	P value	0.988	< 0.001		
SDS Scale Score	Control	74.12 ± 7.15	63.19 ± 6.24	7.726	< 0.001
	Intervention	73.14 ± 7.22	50.23 ± 3.12	19.539	< 0.001
	t value	0.647	12.462		
	Effect size	0.136	2.627		
	P value	0.519	< 0.001		
LES Scale Score	Control	111.59 ± 10.17	77.18 ± 6.25	19.337	< 0.001
	Intervention	110.63 ± 10.14	54.53 ± 2.45	36.075	< 0.001
	t value	0.448	22.634		
	Effect size	0.094	4.772		
	P value	0.655	< 0.001		
WHOQOL-BREF Score	Control	56.44 ± 2.28	77.59 ± 4.32	29.045	< 0.001
	Intervention	56.12 ± 2.34	84.36 ± 5.14	33.543	< 0.001
	t value	0.657	33.308		
	Effect size	0.138	1.426		
	P value	0.513	< 0.001		

SD standard deviation, *MUIS* Mishel uncertainty in illness scale, *SAS* self-rating anxiety scale, *SDS* self-rating depression scale, *LES* life events scale, *WHOQOL-BREF* World Health Organization quality of life scale-brief

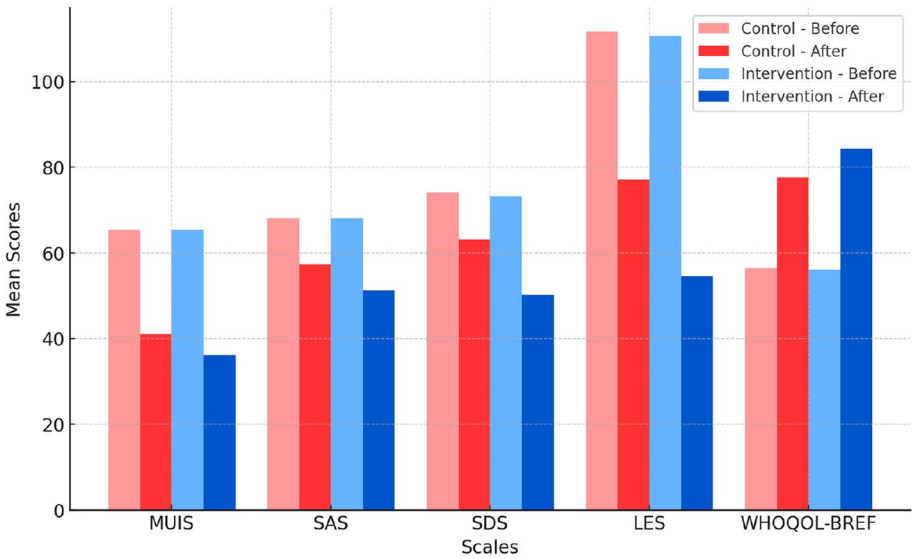

Fig. 2 Study outcomes before and after four cycles of chemotherapy (MUIS: Mishel uncertainty in illness scale, SAS: self-rating anxiety scale, SDS: self-rating depression scale, LES: life events scale, WHOQOL-BREF: World Health Organization quality of life scale-brief)

respecting patient autonomy and empowering them to take an active role in their care. Through cognitive and behavioral interventions, CBT aims to correct maladaptive thought patterns and establish healthy coping mechanisms. Cognitive interventions help patients identify and challenge negative thoughts, reducing disease-related uncertainty and anxiety. Behavioral interventions, such as diaphragmatic breathing, promote physical and mental relaxation by regulating physiological processes and improving overall well-being [39–42]. By addressing both cognitive and behavioral aspects, CBT can effectively alleviate symptoms of anxiety, depression, and stress, and improve the overall quality of life for glioma patients undergoing chemotherapy.

This study conclusively demonstrates the substantial benefits of cognitive behavioral therapy in glioma patients undergoing chemotherapy. CBT is particularly effective in reducing disease-related uncertainty, mitigating the impact of stressful life events, and enhancing overall quality of life. Glioma patients often grapple with fear, anxiety, and uncertainty about their prognosis and future. Low disease awareness and limited coping skills further exacerbate these challenges. Patients may experience negative coping mechanisms, manifesting as anxiety, depression, and restlessness. These psychological factors can hinder treatment adherence and compromise patient outcomes [43, 44].

This study acknowledges several limitations that could potentially affect the generalizability and strength of its findings. The relatively small sample size of 90 patients might not be fully representative of the broader glioma population. A larger sample size could provide more generalizable results and reduce the potential impact of individual variability. The research was conducted in a single hospital (Sanmenxia Central Hospital), which may limit the generalizability of the findings. Different hospitals or healthcare settings might have variations in care practices, which could affect the results. The study only evaluated the effects of cognitive behavioral therapy (CBT) over four chemotherapy cycles. A longer follow-up period would be necessary to assess the long-term benefits and durability of CBT's impact on glioma patients. The study relied heavily on self-reported measures such as the Self-Rating Anxiety Scale (SAS) and the Self-Rating Depression Scale (SDS). These can be subject to response bias, where patients might underreport or overreport symptoms based on their perception. The lack of blinding could introduce bias, as both the patients and the researchers were aware of the group assignments. This might influence the subjective assessments of anxiety, and depression.

Conclusion

The study demonstrated that both groups showed improvement, CBT provided additional benefits in reducing disease uncertainty and psychological distress. Specifically, patients who received CBT showed reduced disease-related uncertainty, lower levels of anxiety and depression. These results suggest that integrating CBT into the standard care for glioma patients can be beneficial in enhancing their overall quality of life during chemotherapy. However, given the limitations of the study, future research with larger, multicenter samples and longer follow-up periods is needed to confirm these findings and explore the sustained impact of CBT interventions. Additionally, incorporating objective measures alongside self-reported scales could provide a more comprehensive evaluation of the therapy's effectiveness.

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Clinical trial number
Not applicable.

Authors' contributions
X.L. and X.Q. were major contributors to conceptualization and writing the manuscript. L.W., D.F., S.F., J.C., X.L., and J.D. collected the patient data and followed up the patients. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Ethics Committee of the The Sanmenxia Central Hospital, Sanmenxia, Henan, China approved the study. All participants were provided with a written informed consent form, clearly stating that their participation in the study was voluntary and that they had the right to withdraw at any time without facing any consequences. The participants were provided with detailed explanations about the confidentiality of their information. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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