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Pharmacological interventions for pain and fatigue management in elderly leukemia patients: A comparative study of analgesic and antidepressant efficacy

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Abstract: Older leukemia patients frequently endure cancer-related pain and fatigue, impairing their daily lives and reducing treatment adherence. Pharmacological intervention is a key approach to alleviating these symptoms. This study focuses on the efficacy and safety of analgesic and anti-fatigue drugs in elderly leukemia patients, aiming to optimize drug selection for precision treatment. From January 2022 to June 2024, Taixing People's Hospital enrolled 82 elderly leukemia patients with pain and fatigue, dividing them into a control group (no analgesics) and a celecoxib group. Clinical outcomes: Pain relief, fatigue reduction, depression improvement, quality of life and adverse reactions were compared at 1, 4, and 8 weeks. The celecoxib group showed significant improvements in pain, fatigue, anxiety, and depression, with better scores on the Numeric Rating Scale (NRS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Edmonton Symptom Assessment System-revised (ESAS-r), the Hospital Anxiety and Depression Scale-Anxiety (HADS-A) and the Hospital Anxiety and Depression Scale-Depression (HADS-D) scales at all-time points (P<0.05). Their Quality of Life Questionnaire Core 15 Palliative (QLQ-C15-PAL) scores also indicated enhanced functional and overall quality of life, with lower symptom scores compared to the control group (P<0.05). No serious adverse events occurred, confirming celecoxib's safety.

Keywords: Celecoxib; Elderly patients; Fatigue; Leukemia; Pain

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INTRODUCTION

Leukemia, a malignant hematopoietic stem cell disease characterized by uncontrolled white blood cell proliferation and infiltration in bone marrow and related tissues, suppresses normal blood cell production, manifesting as anemia, bleeding, infections and organ enlargement (Whiteley *et al.*, 2021). Its etiology involves genetic and environmental factors. Leukemia is classified into four main types: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myelogenous leukemia (CML). Terminal-stage leukemia often leads to multi-organ dysfunction and pain (Mu *et al.*, 2023). Leukemia is a significant global health issue, ranking 13th in cancer incidence and 10th in cancer-related deaths (Bray *et al.*, 2024). The aging population has increased leukemia incidence among the elderly (Vetrie *et al.*, 2020), who exhibit unique disease onset characteristics, including insidious onset, atypical initial symptoms, frequent comorbidities, susceptibility to infections or bleeding, prolonged bone marrow suppression and high mortality (Tang *et al.*, 2024). Due to declining organ function, elderly patients often cannot undergo stem cell transplantation. Clinical treatment goals focus on extending lifespan and improving quality of life (Edmund *et al.*, 2023). Chemotherapy and molecular targeted therapy are primary treatments but are associated with side effects. The combined impact of disease and treatment pain, coupled with declining physical function, often leads to distorted life perceptions, depression and despair, reducing treatment adherence and quality of life (Choi *et al.*, 2023).

Leukemia patients frequently experience pain due to disease progression or treatment side effects (Emamian *et al.*, 2023). According to the International Association for the Study of Pain (IASP), pain is a complex physiological and psychological phenomenon characterized by unpleasant sensations and emotions linked to actual or potential tissue damage (Ito *et al.*, 2022). Elderly leukemia patients exhibit distinct pain generation and perception traits owing to physiological and psychological factors, including reduced pain sensitivity from neurodegenerative changes, heightened susceptibility to chronic pain and comorbidities (Flynn *et al.*, 2022) and diminished drug metabolism and analgesic tolerance, complicating pain management (Tinnirello *et al.*, 2021). Cancer-related fatigue, a common, persistent and distressing symptom among cancer patients and survivors (Wang *et al.*, 2023), is highly prevalent in leukemia patients, with incidence rates up to 89% (AlFayyad *et al.*, 2020). This fatigue manifests as unremitting exhaustion resistant to rest or sleep, significantly impacting quality of life, emotions, cognitive function and treatment outcomes (Kang *et al.*, 2023; Ma *et al.*, 2020). Elderly patients, due to declining physical functions, have reduced illness tolerance, increased chemotherapy side effect susceptibility and heightened infection risks from immune system

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deterioration, all of which exacerbate cancer-related fatigue (Özdemir and Taşcı, 2023). Despite the widespread clinical use of medications for symptomatic treatment in leukemia, existing research inadequately addresses the specific efficacy and safety of analgesic and anti-fatigue drugs in elderly leukemia patients. Pharmacological interventions for cancer-related fatigue remain under-researched, with a lack of high-level evidence validating their effectiveness (Sandford *et al.*, 2023). Painkillers, primarily used to alleviate cancer-induced pain, a key contributor to fatigue, may indirectly mitigate fatigue by reducing pain (Wang *et al.*, 2023). The World Health Organization (WHO) three-step ladder approach is commonly employed for cancer pain management, yet adverse reactions often compromise pain control as treatment advances (Yazdani *et al.*, 2021). Clinical experience indicates that non-steroidal anti-inflammatory drugs (NSAIDs) provide effective analgesia with reduced side effects and improved patient adherence (Rashid *et al.*, 2023). Celecoxib, a selective COX-2 inhibitor, demonstrates fewer gastrointestinal adverse effects compared to traditional NSAIDs (Ahmadi *et al.*, 2022). Emerging evidence suggests analgesics may improve cognitive function and alleviate cancer-related fatigue; for instance, dexamethasone reduced fatigue, nausea, appetite loss, depression and sleep disturbances in a trial, enhancing quality of life by day 15 (Yennurajalingam *et al.*, 2013). However, inconsistent findings due to sample variability, research design diversity and outcome measurement discrepancies necessitate further investigation before widespread analgesic use for cancer-related fatigue to secure reliable evidence. Therefore, the objective of this study is to evaluate the efficacy and safety of celecoxib in managing cancer-related pain and fatigue, and its impact on depression, anxiety, and quality of life in elderly patients with leukemia.

MATERIALS AND METHODS

Design

This study is a retrospective clinical controlled study conducted at the Geriatrics Department of the Taixing People's Hospital. The designed operational flow is shown in fig. 1. A total of 110 elderly leukemia patients from January 2022 to June 2024 were selected, among whom 82 patients met the inclusion and exclusion criteria. The cohort was stratified into two groups: 42 in the celecoxib group, receiving celecoxib for analgesia and 40 in the control group, not receiving any analgesic medication. All patients were followed up.

Participants

From January 2022 to June 2024, 82 leukemia patients were enrolled in the Taixing People's Hospital as study subjects. Inclusion criteria: Age≥60 years; diagnosis of leukemia confirmed according to the diagnostic criteria established by the WHO through peripheral blood routine tests, bone marrow aspiration, bone marrow biopsy, cytogenetics, molecular biology, etc. (Xiao *et al.*, 2024); patients with accompanying pain; fulfilling the diagnostic criteria for cancer-related fatigue as outlined in the International Classification of Diseases, Tenth Revision (ICD-10) (Rau *et al.*, 2020); predicted survival time of more than 3 months to ensure patients have sufficient time to benefit from treatment; patients with normal communication skills who can understand and cooperate with the treatment plan. Exclusion criteria: Allergy or contraindication to the treatment drugs used in this study; severe organ dysfunction, such as heart, liver, kidney, or other organ failure; concurrent other malignant tumors; concurrent severe neurological diseases; incomplete medical and nursing records, making it impossible to assess the patient's condition and treatment effect.

Intervention

The study population was stratified into two cohorts based on the treatment modality, with 42 patients comprising the celecoxib group who received celecoxib for analgesic treatment. The control group included 40 patients who did not receive any analgesic medication. Celecoxib (capsule, 0.2g; Import Drug License H20140106; manufactured by Pfizer Inc., USA) was orally administered twice daily, at a dosage of 200 mg each time. The comparative clinical efficacy of the two groups was assessed at 1, 4 and 8 weeks post-treatment. The pain levels of patients in the control group were closely monitored. Rescue analgesics were provided to patients who experienced uncontrollable severe pain to ensure their comfort.

Sample size calculation

Since no similar studies have been conducted before, this study used the numeric rating scale (NRS) score data from the first 20 elderly leukemia patients enrolled to calculate the sample size. After estimation, this study concluded that to ensure the accuracy and reliability of the study (i.e., controlling the risk of type I error within 0.05 and achieving a statistical power of 90%), at least 35 elderly leukemia patients were required to participate in each group. This study meets the sample size requirement.

Blinding implementation

This study used a single-blind design and participants were unaware of their group assignment (celecoxib or control group) to minimize subjective bias. The double-blind design was not feasible for the researchers due to the nature of the intervention. However, data analysis was performed by investigators who were not involved in the conduct of the experiment to ensure the objectivity of the results.

Outcome measures

Record the demographic and clinical data of the patients, including age, gender, race, cancer diagnosis and treatment history. The primary outcomes include the improvement in pain and fatigue in the two patient groups. (1) Pain in elderly leukemia patients is assessed using the NRS

(Bielewicz *et al.*, 2022). Patients were instructed to select a number on a scale of 0 to 10 that best represented their pain level. (2) The assessment of fatigue in elderly leukemia patients is conducted using the 13-item Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale (Delgado-Álvarez *et al.*, 2022). This instrument evaluates the patient's fatigue level and its consequences on daily functioning, utilizing a 5-point Likert scale (ranging from 0 to 4 points) for each item. The total score of the questionnaire spans from 0 to 52, where higher scores reflect lesser fatigue severity.

The secondary outcomes encompass enhancements in depression symptoms, quality of life and medication-related adverse reactions among the two patient cohorts. (1) The Edmonton Symptom Assessment System-revised (ESAS-r) (Afsar *et al.*, 2023) is used to assess the severity of 10 common symptoms in patients, including pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, well-being and constipation. The ESAS-r employs a 0-10 rating scale for individuals to indicate the severity of each symptom they experience. The cumulative symptom burden score can range from 0 to 100, with higher scores reflecting greater symptom severity. The ESAS-r is frequently utilized for monitoring symptom fluctuations and aiding healthcare providers in tailoring treatment strategies. (2) The Hospital Anxiety and Depression Scale (HADS) (Annunziata *et al.*, 2020) is a self-assessment scale used to evaluate anxiety and depression symptoms in patients within a medical environment.

The instrument comprises two subscales: The HADS-Anxiety (HADS-A) and the HADS-Depression (HADS-D), encompassing a total of 14 items. Each item is scored on a 4-point scale ranging from 0 to 3, yielding a total possible score between 0 and 21. (3) The Quality of Life Questionnaire Core 15 Palliative (QLQ-C15-PAL) questionnaire (Pilz *et al.*, 2021), developed by the European Organisation for Research and Treatment of Cancer (EORTC). It serves as a crucial instrument for evaluating the quality of life among cancer patients undergoing palliative care. The questionnaire encompasses 15 items, categorized into two functional domains ("Physical Functioning" and "Emotional Functioning") and seven symptom domains ("Fatigue," "Nausea/Vomiting," "Pain," "Dyspnea," "Insomnia," "Appetite Loss," "Constipation"), alongside an overall quality of life domain. Responses are based on patients' experiences over the past week. Most items utilize a 4-point scale ranging from 1 ("Not at all") to 4 ("Very much"), while the overall quality of life is assessed on a 7-point scale spanning from 1 ("Very poor") to 7 ("Excellent"). All domains undergo linear transformation, resulting in scores between 0 and 100. Higher scores in the functional and overall quality of life domains signify better health-related quality of life, whereas higher scores in the symptom domains indicate greater symptom severity. (4) Patients are asked weekly about the occurrence of known potential adverse events, which are categorized as mild, moderate, or severe based on their severity. Severe adverse events need to be reported and documented separately. Classification Specific Criteria: Mild adverse effects: refer to adverse reactions that cause mild discomfort or symptoms and do not affect the patient's daily activities, usually requiring no special treatment or intervention. Moderate adverse effects: refer to adverse reactions that cause noticeable discomfort or symptoms and may interfere with some daily activities, possibly necessitating symptomatic treatment or minor adjustments to the treatment regimen. Severe adverse effects: refer to adverse reactions that cause significant discomfort or symptoms and severely impact the patient's daily activities, potentially requiring major medical interventions such as adjustments to the treatment regimen, hospitalization, or other significant measures.

Statistical analysis

Data analyzed by SPSS 25.0. Normal data as $\overline{x}\pm s$, t-test; non-normal data as [M(Q1, Q3)], Mann-Whitney U test; categorical data as n (%), χ^2 test. $P<0.05$ was considered statistically significant.

RESULTS

Comparison of baseline characteristics

The χ^2 test was used to compare gender, education level, marital status and leukemia type between the control group and the celecoxib group. Age and disease duration followed a normal distribution and were compared using an independent sample t-test. No statistically significant differences were observed in the baseline demographic characteristics or diagnostic types between the two groups ($P>0.05$), ensuring the comparability of subsequent intervention effects (Table 1).

Changes in pain intensity over time in elderly patients with leukemia

Over time, the cancer-related pain intensity in patients in the celecoxib group was significantly alleviated compared to before medication and the NRS scores at various time points were significantly lower than those in the control group, with a statistically significant difference ($P<0.05$) (Table 2)

Changes in fatigue levels over time in elderly patients with leukemia

During the continuous observation period, as the duration of medication increased, patients in the celecoxib group experienced significant relief in their fatigue levels compared to before medication. Compared with the control group, the FACIT-F scores of the celecoxib group were higher at each time point, with a statistically significant difference between the two groups ($P<0.05$) (Table 3)

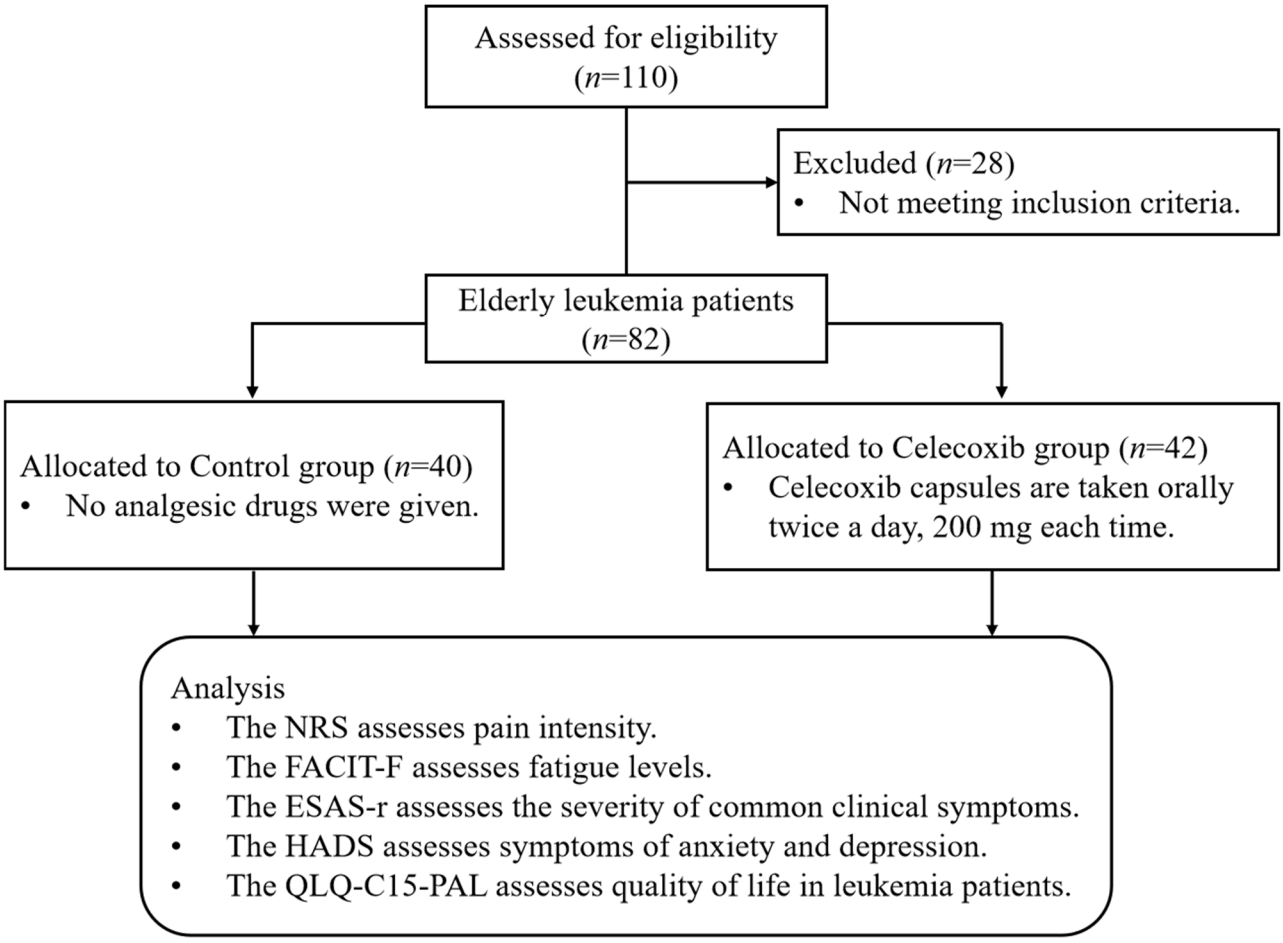

Fig. 1: Design operation process

Table 1: Comparison of baseline characteristics

Characteristic	Control group (*n*=40)	Celecoxib group (*n*=42)	χ^2/t	*P*
Age ($\overline{x}\pm s$, years)	67.63±6.86	68.74±6.66	0.745	0.458
Sex (n,%)				
Male	17 (42.50)	18 (42.86)	0.001	0.974
Female	23 (57.50)	24 (57.14)		
Marital status (n,%)				
Divorced/single	8 (20.00)	7 (16.67)	0.152	0.696
Married	32 (80.00)	35 (83.33)		
Education level (n,%)				
Below high school	21 (52.50)	20 (47.62)	0.195	0.659
High school and above	19 (47.50)	22 (52.38)		
Diagnosis (n,%)				
ALL	4 (10.00)	5 (11.90)	0.204	0.977
AML	18 (45.00)	19 (45.24)		
CLL	11 (27.50)	10 (23.81)		
CML	7 (17.50)	8 (19.05)		
Course of disease ($\overline{x}\pm s$, months)				
0~3	21 (52.50)	23 (54.76)	0.159	0.924
4~12	12 (30.00)	13 (30.95)		
>12	7 (17.50)	6 (14.29)		

Changes in clinically common symptoms over time in elderly patients with leukemia

Throughout the entire observation period of the study, as the duration of medication increased for patients in the celecoxib group, their various clinically common symptoms showed a significant trend of alleviation compared to before medication. In dynamic monitoring at different time points, the ESAS-r scores of the celecoxib group were significantly lower compared to the control group, with a statistically significant difference between the two groups (P<0.05) (Table 4).

Changes in anxiety and depression over time in elderly patients with leukemia

Throughout the continuous observation period of the study, as the duration of medication for patients in the celecoxib group continued to increase, their anxiety and depression status showed significant improvement compared to the baseline levels before medication. Assessment results at various time points indicated that the HADS-A and HADS-D scores of the celecoxib group were significantly lower than those of the control group, with a statistically significant difference between the two groups (P<0.05) (Table 5)

Changes in quality of life over time in elderly patients with leukemia

Over time, the quality of life of patients in the celecoxib group showed significant improvement compared to before medication. At each time point, the QLQ-C15-PAL scores for functional scales and overall quality of life were significantly higher in the celecoxib group than in the control group, while the symptom scores were significantly lower. The differences between the groups were statistically significant (P<0.05) (Table 6)

Adverse reactions

Under rigorous monitoring and assessment, no serious adverse events were reported by participants in both groups. Notably, while no severe adverse events were documented in the celecoxib group, some minor side effects were observed. These included occasional gastrointestinal discomfort, such as mild dyspepsia or nausea, experienced by three patients. However, these side effects were generally mild and did not warrant discontinuation of celecoxib treatment. This outcome suggests that celecoxib exhibits good safety in clinical practice and does not pose a significant negative threat to the overall health of the participants (Table 7).

DISCUSSION

Our study enrolled 82 elderly leukemia patients with balanced baseline characteristics between the celecoxib and control groups. No significant differences were observed in age, sex, marital status, education level, leukemia subtypes, or disease duration (all P>0.05), ensuring that the observed outcomes were unlikely to be confounded by these variables. Notably, the majority of participants had AML or CLL, which may be associated with distinct pain and fatigue profiles due to differences in disease biology. However, the balanced distribution of subtypes between groups supports the generalizability of our findings across common leukemia types in the elderly. This research evaluated and contrasted the effectiveness and safety profile of celecoxib versus a control group in the elderly patient population with leukemia, delving into the role of analgesic medications in alleviating cancer-related pain and cancer-related fatigue. The research results indicate that celecoxib not only significantly improved patients' pain and fatigue symptoms but also demonstrated remarkable advantages in alleviating anxiety, depression and enhancing quality of life. This finding provides important clinical evidence for the comprehensive treatment of elderly patients with leukemia and also prompts further consideration of symptom management and drug intervention strategies for cancer patients.

Cancer-associated pain is a prevalent symptom in elderly leukemia patients and its incidence is intimately linked to leukemia cell infiltration, inflammatory reactions and therapeutic interventions. Leukemia cell infiltration stands as a primary contributor to the onset of pain. Leukemia cells have high invasiveness and proliferative capacity, enabling them to infiltrate and affect multiple parts of the body, including the bone marrow, bones, joints, internal organs and central nervous system, causing inflammatory reactions and compressive symptoms in local tissues (Wang *et al.*, 2024). For example, the massive proliferation of leukemia cells in the bone marrow can lead to increased pressure within the bone marrow cavity, stimulating the periosteum and surrounding nerve endings, resulting in persistent dull pain or severe pain (Siddiqi *et al.*, 2022). Additionally, the increased pressure in the bone marrow cavity not only stimulates nerve endings but also activates nociceptors beneath the periosteum, which are highly sensitive to mechanical pressure and chemical stimuli. When stimulated, these nociceptors transmit pain signals to the central nervous system, generating a sensation of pain (Slouma *et al.*, 2023).

Furthermore, cytokines released by leukemia cells, such as Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α), can also activate nociceptors and increase the excitability of primary afferent neurons, making pain signals more easily transmitted and exacerbating the pain (Tanaka *et al.*, 2021). At the same time, chemotherapy drugs kill cancer cells by inhibiting rapidly dividing cells, but due to their lack of selectivity, they can also damage other rapidly dividing normal cells, including those in bones and joints, further triggering pain (Seymour *et al.*, 2023). Celecoxib, as a selective COX-2 inhibitor, exerts its analgesic action by suppressing prostaglandin synthesis and decreasing the secretion of inflammatory mediators

(Saxena *et al.*, 2020). The findings of this study indicated that the NRS scores for patients in the celecoxib group were statistically significantly lower compared to those in the control group at weeks 1, 4 and 8 after medication, indicating its clear efficacy in alleviating cancer-related pain. COX-2 is highly expressed in the inflammatory and tumor microenvironment and is closely related to inflammatory responses and pain signal transmission, being responsible for catalyzing the synthesis of prostaglandins, which are key molecules mediating pain and inflammation (Cui and Jia, 2021). As a COX-2 inhibitor, celecoxib can significantly reduce the levels of prostaglandin E2 (PGE2), a potent pain-inducing mediator that directly stimulates pain receptors and enhances neural sensitivity to pain signals (Ashrafizadeh, 2024; Bedoui *et al.*, 2021). Chronic pain can lead to central sensitization of the central nervous system, where central neurons become more sensitive to pain signals. Celecoxib alleviates chronic pain by inhibiting COX-2 expression in the central nervous system, thereby reducing central sensitization (Blichfeldt-Eckhardt *et al.*, 2022). Studies have shown that celecoxib inhibits tumor cell proliferation, metastasis and lymphangiogenesis by inhibiting Signal Transducer and Activator of Transcription 3 (STAT3) phosphorylation [related to the Janus Kinase-STAT3 (JAK-STAT) signaling pathway] and downregulating Vascular Endothelial Growth Factor-C (VEGF-C) expression (Ji *et al.*, 2024; Makabe *et al.*, 2024; Ren, 2024).

This anti-tumor activity may reduce the compression or nerve infiltration of surrounding tissues by the tumor, thereby alleviating pain. Elderly patients with leukemia often have multiple underlying diseases and decreased physiological function, making pain management more challenging. Compared with traditional non-selective NSAIDs (such as ibuprofen and naproxen), celecoxib has a weaker inhibitory effect on COX-1, thus causing less gastrointestinal irritation and reducing the risk of gastrointestinal bleeding and ulcers (Cruz *et al.*, 2022). This is particularly important for elderly patients, who are usually more sensitive to gastrointestinal adverse reactions. In addition, elderly patients often need to take multiple medications and celecoxib is primarily metabolized by the Cytochrome P450 2C9 (CYP2C9) enzyme in the liver, with fewer interactions with other drugs, reducing the risk of multidrug combination therapy (Kim *et al.*, 2021). Although no serious adverse events were reported in this study, patients' cardiovascular health status still needs to be closely monitored in clinical applications, especially for elderly patients who may have multiple underlying diseases, making drug safety particularly important.

Cancer-related fatigue is another major concern for elderly patients with leukemia, with the disease itself and its treatment being the primary contributors (Cho *et al.*, 2023; Liu and Wang, 2024). Leukemia cells inhibit the production of normal red blood cells, reducing their number in the blood and consequently impairing oxygen transport capacity, leading to persistent fatigue and a sense of weakness in patients (Alibhai *et al.*, 2020). Additionally, hormones released by leukemia cells, inflammatory cytokines, immune system dysregulation and hypothalamic-pituitary-adrenal (HPA) axis malfunction may both contribute to the onset of cancer-related fatigue (Zhang and Wang, 2024). Chemotherapy constitutes a primary therapeutic modality for leukemia; however, it non-selectively eliminates both tumor and normal cells, leading to adverse effects such as bone marrow suppression, anemia and malnutrition, which in turn can trigger or exacerbate cancer-related fatigue (Medeiros Torres *et al.*, 2022). Furthermore, chemotherapy may also induce immune system disorders, reducing patients' immunity and further intensifying their fatigue. Cancer-related fatigue not only causes leukemia patients to exhibit symptoms such as persistent fatigue, weakness, lethargy, cognitive impairment and low mood, but these symptoms also severely impact patients' daily lives and treatment outcomes (Ee *et al.*, 2024). Moreover, cancer-related fatigue may exacerbate complications such as anemia, malnutrition and sleep disorders, further deteriorating patients' quality of life (Wang *et al.*, 2024). The results of this study demonstrated a significant improvement in FACIT-F scores among patients in the celecoxib group, highlighting its notable efficacy in mitigating cancer-related fatigue.

The potential mechanism underlying celecoxib's alleviation of cancer-related fatigue may be intricately linked to its anti-inflammatory properties. Cancer-related fatigue is intimately tied to chronic inflammation, where inflammatory cytokines within the tumor microenvironment facilitate tumor progression and metastasis while also inducing fatigue through various pathways. Specifically, cytokines such as IL-6 and TNF-α can traverse the blood-brain barrier to directly impact the hypothalamus, stimulating the release of corticotropin-releasing hormone and subsequently disrupting HPA axis function. This disruption affects glucose metabolism, lipid breakdown and protein synthesis, ultimately leading to energy deprivation and the onset of fatigue. As a selective COX-2 inhibitor, celecoxib effectively decreases the levels of these inflammatory cytokines. In addition, inflammatory responses are often accompanied by increased oxidative stress, which can damage mitochondrial function in cells, leading to energy metabolism disorders. By inhibiting COX-2, celecoxib reduces oxidative stress, thereby improving energy metabolism and alleviating fatigue. Pain and mood disorders (such as anxiety and depression) are important contributors to cancer-related fatigue (Grusdat *et al.*, 2022). Chronic pain can lead to sleep disturbances and decreased activity levels, further exacerbating fatigue. Celecoxib indirectly alleviates fatigue by relieving pain and improving emotional status.

Table 2: Comparison of NRS scores

Observation time point	Control group (*n*=40)	Celecoxib group (*n*=42)	*Z*	*P*
Baseline	4.5 (4, 5)	5 (4, 5)	-1.120	0.263
Week 1	4 (4, 5)	3 (2, 4)	-4.866	0.000
Week 4	5 (4, 5)	2 (2, 3)	-8.467	0.000
Week 8	4 (3, 5)	2 (1, 2)	-8.217	0.000

Table 3: FACIT-F score comparison

Observation time point	Control group (*n*=40)	Celecoxib group (*n*=42)	*t*	*P*	*95% CI*
Baseline	24.65±4.17	24.57±4.55	0.084	0.935	-1.843 ~ 2.000
Week 1	24.48±4.39	28.64±2.18	5.487	0.000	-5.679 ~ -2.656
Week 4	23.55±4.23	32.71±3.35	10.901	0.000	-10.837 ~ -7.491
Week 8	24.98±3.18	39.29±3.42	19.602	0.000	-15.764 ~ -12.858

Table 4: Comparison of ESAS-r scores

Observation time point	Control group (*n*=40)	Celecoxib group (*n*=42)	*t*	*P*	*95% CI*
Baseline	40.88±5.22	41.71±4.94	0.748	0.457	-3.072 ~ 1.393
Week 1	38.23±4.54	32.52±4.47	5.728	0.000	3.721 ~ 7.682
Week 4	39.55±3.69	27.74±3.68	14.497	0.000	10.191 ~ 13.433
Week 8	40.23±4.85	21.29±3.54	20.251	0.000	17.078 ~ 20.800

Table 5: Comparison of HADS scores

Observation time point		Control group (*n*=40)	Celecoxib group (*n*=42)	*t*	*P*	*95% CI*
HADS-A	Baseline	16.65±1.75	16.48±1.53	0.479	0.633	-0.548 ~ 0.896
	Week 1	16.58±1.52	14.50±1.50	6.222	0.000	1.411 ~ 2.739
	Week 4	16.78±1.85	11.36±1.69	13.856	0.000	4.640 ~ 6.196
	Week 8	16.42±1.77	8.21±1.47	23.002	0.000	7.500 ~ 8.921
HADS-D	Baseline	15.45±1.77	15.71±1.71	0.687	0.494	-1.030 ~ 0.501
	Week 1	15.23±1.67	13.33±1.28	5.768	0.000	1.239 ~ 2.544
	Week 4	14.98±1.66	10.88±1.52	11.680	0.000	3.396 ~ 4.792
	Week 8	15.15±1.70	7.45±1.56	21.328	0.000	6.979 ~ 8.416

Table 6: Comparison of QLQ-C15-PAL scores

Observation time point		Control group (*n*=40)	Celecoxib group (*n*=42)	*Z*	*P*
Functional scales	Baseline	20.00 (13.33, 20.00)	16.67 (8.34, 20.00)	-0.715	0.474
	Week 1	13.33 (13.33, 20.00)	40.00 (26.67, 46.67)	-5.927	0.000
	Week 4	13.33 (6.67, 20.00)	60.00 (48.34, 71.67)	-7.829	0.000
	Week 8	13.33 (6.67, 18.33)	73.33 (66.67, 80.00)	-7.879	0.000
Symptom scales	Baseline	61.11 (55.56, 62.96)	62.96 (55.56, 62.96)	-0.405	0.686
	Week 1	61.11 (55.56, 62.96)	51.85 (48.15, 55.56)	-5.423	0.000
	Week 4	59.26 (56.49, 62.96)	37.04 (33.33, 40.74)	-7.864	0.000
	Week 8	62.96 (55.56, 66.67)	29.63 (22.22, 33.33)	-7.852	0.000
Overall quality of life	Baseline	33.33 (16.67, 33.33)	33.33 (16.67, 33.33)	-0.119	0.905
	Week 1	33.33 (16.67, 33.33)	50.00 (50.00, 50.00)	-7.100	0.000
	Week 4	33.33 (16.67, 33.33)	50.00 (50.00, 50.00)	-6.605	0.000
	Week 8	33.33 (20.84, 33.33)	66.67 (66.67, 83.33)	-7.867	0.000

Table 7: Comparison of adverse reactions

Adverse Reactions	Control group (*n*=40)	Celecoxib group (*n*=42)	χ^2	*P*
Nausea	0 (0.00)	1 (2.38)		
Vomiting	0 (0.00)	1 (2.38)		
Abdominal pain	0 (0.00)	1 (2.38)		
Total	0 (0.00)	3 (7.14)	1.285	0.257

Studies have shown that there is a bidirectional relationship between mood disorders and fatigue and improving emotional status can help reduce fatigue (Rodriguez-Gonzalez *et al.*, 2022). It is worth noting that cancer-related fatigue is a multidimensional symptom and its management requires comprehensive interventions.

Although celecoxib has shown significant effects in alleviating cancer-related fatigue, its role may be limited. Future research can explore the combined use of celecoxib with other interventions (such as psychological support and exercise therapy) to further enhance its efficacy.

The ESAS-r scores revealed significant reductions in symptom burden among celecoxib-treated patients, particularly for tiredness, nausea and dyspnea. This aligns with the known anti-inflammatory effects of COX-2 inhibition, which may mitigate cytokine-driven symptoms, such as IL-6-induced fatigue and TNF-α-related nausea (Ballaz and Bourin, 2023; Ju *et al.*, 2023). Importantly, the control group exhibited stagnant or worsened ESAS-r scores over time, suggesting that untreated pain and inflammation exacerbate systemic symptoms in leukemia. This underscores the potential of celecoxib not only for pain relief but also for broader palliative benefits.

The HADS results demonstrated marked improvements in HADS-A and HADS-D scores in the celecoxib group, while the control group showed persistent psychological distress. This divergence may be attributed to celecoxib's dual role: direct modulation of neuroinflammatory pathways, such as COX-2/PGE2 axis in limbic system and indirect effects via pain and fatigue relief, which are established contributors to mood disorders in cancer patients (Ouyang *et al.*, 2024; Qi *et al.*, 2023). In contrast, the absence of analgesic intervention in the control group likely perpetuated a cycle of unrelieved symptoms and psychological deterioration, highlighting the importance of integrated symptom management in leukemia care. Quality of life serves as a crucial metric for evaluating treatment efficacy in cancer patients.

The findings of this study revealed a significant enhancement in QLQ-C15-PAL scores among patients in the celecoxib group, characterized by elevated functional scores and overall quality of life scores in comparison to the control group, as well as reduced symptom scores relative to the control group. These results indicate that celecoxib has a significant effect on improving the quality of life of elderly leukemia patients. The mechanism by which celecoxib improves quality of life may be related to its comprehensive improvement of pain, fatigue and emotional status. Pain and fatigue are the main factors affecting the quality of life of cancer patients and mood disorders further exacerbate the patients' suffering. By alleviating these symptoms, celecoxib significantly improves the patients' quality of life.

Limitations of the study

This study has several limitations. As a single-center study with strict exclusion criteria and a small sample size, its findings may lack generalizability to real-world elderly leukemia patients, who often have comorbidities and the restricted sample increases selection bias. The 8-week follow-up period is insufficient to assess long-term outcomes like chronic pain management, fatigue recurrence and late-onset adverse effects, necessitating future studies with follow-ups of 6-12 months. The retrospective design risks selection bias, unmeasured confounders and incomplete data, while the lack of randomization and blinding may introduce performance and detection bias, warranting prospective, randomized, blinded designs in future research. Additionally, the absence of a placebo or standard-care control group may bias results and raise ethical concerns, highlighting the need for comparative controls in subsequent studies. Finally, the analysis did not stratify by leukemia subtype, chemotherapy regimens, or comorbidities-key factors influencing pain and fatigue-suggesting future work should incorporate subgroup analyses to better capture treatment-response variations. Addressing these limitations would strengthen evidence on celecoxib's role in leukemia care.

CONCLUSION

Our study demonstrates that celecoxib significantly alleviates pain, fatigue, anxiety and depression while improving quality of life in elderly leukemia patients, with a favorable safety profile. For clinical nurses, we recommend considering celecoxib as first-line adjunctive therapy for managing cancer-related symptoms in this population while monitoring for potential gastrointestinal and cardiovascular effects. Patients should be encouraged to report symptom changes promptly and combine medication with non-pharmacological approaches like light exercise. These findings support incorporating COX-2 inhibitors into comprehensive palliative care for elderly leukemia patients, though further randomized trials comparing celecoxib with standard analgesics are needed to confirm long-term benefits.

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Authors' contribution
Qin Li: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions.
Xin Sun: Participated in collecting, assessing and interpreting the data. Made significant contributions to date interpretation and manuscript preparation.

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Data availability statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval
This study was approved by the Ethics Committee of the Taixing People's Hospital. Written informed consent was secured from every participant, ensuring full transparency and voluntary participation (Approval No. LS2025031-2).

Consent to publish
The manuscript has neither been previously published nor is it under consideration by any other journal. The authors have all approved the content of the paper.

Consent to participate
We secured a signed informed consent form from every participant.

Conflict of interest
The authors declare that they have no financial conflicts of interest.

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