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RESEARCH

Clinical efficacy of compression therapy in preventing oxaliplatin-induced peripheral neuropathy: a prospective, randomized controlled study

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Abstract

Purpose This study aims to evaluate the efficacy of compression therapy in preventing oxaliplatin-induced peripheral neuropathy (OIPN) in colorectal cancer patients.

Methods Colorectal cancer patients scheduled for their first oxaliplatin-based chemotherapy were randomly assigned to a compression therapy group or a control group. The control group received standard care, while the compression therapy group wore grade II (23–32 mmHg) compression sleeves and socks from 30 min before to 30 min after oxaliplatin infusion. Sensory and motor neuropathy incidence and symptom burden were assessed using physician evaluations and patient self-reports. Adverse events during the treatment period were also recorded.

Results After four cycles, the compression therapy group had a significantly lower incidence of grade ≥ 2 sensory and motor neuropathy compared to the control group (sensory: 41.4% vs. 80.6%, $P=0.002$; motor: 34.5% vs. 67.7%, $P=0.010$). EORTC QLQ-CIPN20 scores were also significantly lower in the compression therapy group after the third and fourth cycles ($P<0.05$). Longitudinal analysis using a mixed-effects model showed a statistically significant difference in the trend of increasing OIPN incidence between the two groups (sensory: $OR=0.294$, $P=0.001$; motor: $OR=0.265$, $P=0.001$). Additionally, the compression therapy group had significantly lower EORTC QLQ-CIPN20 scores ($\beta=-2.157$, 95% CI = [−3.050, −1.264], $P<0.001$). No adverse events related to compression therapy were observed.

Conclusion Compression therapy reduces the incidence and severity of oxaliplatin-induced peripheral neuropathy in colorectal cancer patients and is safe and feasible, warranting further research.

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Keywords Colorectal cancer · Oxaliplatin · Chemotherapy · Peripheral neuropathy · Compression therapy

Xiaotao Zhang and Le Yu contributed equally to this work and should be regarded as the co-first author.

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Introduction

Platinum-based drugs are the frontline treatment for many malignancies, particularly occupying a pivotal role in the treatment of colorectal and gastric cancers [1]. Chemotherapy-induced peripheral neuropathy (CIPN) is a common adverse effect of cancer therapy [2], predominantly associated with platinum-based drugs, especially with the highest incidence of neuropathy observed in patients treated with oxaliplatin. Studies suggest that up to 94% of patients treated with oxaliplatin-based regimens may experience varying degrees of neuropathy [3]. Clinically, oxaliplatin-induced peripheral neuropathy (OIPN) manifests as abnormalities in

sensory and motor nerves, with sensory disturbances such as numbness and hypersensitivity to cold being predominant. These symptoms, which distribute symmetrically and peripherally in a "glove and stocking" pattern, start from the fingers and toes and potentially progress toward the proximal limbs, accompanied by the disappearance of tendon reflexes or motor coordination issues [4]. It is worth noting that oxaliplatin-induced peripheral neuropathy (OIPN) can be classified into acute and chronic forms. Acute OIPN typically emerges within hours after chemotherapy administration and reaches its peak intensity within 2 to 3 days [5]. The progression and severity of OIPN are dose-dependent and gradually worsen with continued antitumor therapy, eventually developing into chronic OIPN, resulting in dose reductions or treatment discontinuation and ultimately impairing patients' quality of life and overall survival [6]. Moreover, the symptoms of acute neuropathy do not always fully resolve between treatment cycles, and there is a reported correlation between the severity of acute and chronic neuropathy [5].

The Oncology Nursing Society highlighted the importance of addressing CIPN in cancer care as early as 2009 [6]. However, to date, no medication has been proven to offer significant neuroprotection for patients with CIPN. According to the latest clinical practice guidelines for CIPN by the American Society of Clinical Oncology (ASCO) [7] and the European Society for Medical Oncology (ESMO) [8], only duloxetine has shown limited benefits in the treatment of CIPN pain. However, due to its side effects, it has received only a moderate recommendation. For severe CIPN, reducing chemotherapy drug dosage or stopping chemotherapy altogether is still advised to alleviate symptoms, further reducing the quality of life [9].

Given the lack of effective pharmacological options, external treatment methods are garnering increasing attention among researchers. At a clinical trial projects meeting hosted by the National Cancer Institute [10], experts highlighted the importance of further research into external treatments aimed at reducing or delaying the onset of CIPN. Cryotherapy involves wearing cold gloves and socks before to after the infusion of chemotherapy drugs, leading to vasoconstriction in the extremities. This process lowers the concentration of chemotherapeutic agents in peripheral tissues, thereby reducing both the incidence and severity of CIPN [11, 12]. However, this method faces issues such as poor tolerance, high dropout rates, lengthy preparation time, and high costs. Inspired by the mechanisms of cryotherapy, compression therapy emerged as an alternative, leveraging mechanical pressure to transiently reduce extremity blood flow during chemotherapy infusion, thereby mitigating neurotoxic drug exposure to peripheral nerves [13]. Preliminary studies on compression therapy have demonstrated its potential in alleviating peripheral neuropathy (PN) caused by taxanes [14, 15]. Nevertheless, these studies were not randomized controlled trials (RCTs) and primarily involved patients receiving taxane-based chemotherapy, indicating a need for further evidence-based research and controlled trials to establish the efficacy of compression therapy.

Although taxane- and oxaliplatin-induced neuropathies arise from different primary mechanisms, with microtubule disruption associated with taxanes and ion-channel dysfunction and dorsal root ganglion toxicity associated with oxaliplatin, both agents exhibit a common feature. Studies have shown that these agents produce a length-dependent distal-to-proximal gradient of neurotoxicity, with greater drug exposure in distal axons leading to more severe nerve damage [16, 17]. Based on this rationale, we designed a prospective randomized controlled trial to evaluate the clinical efficacy of compression therapy in preventing OIPN. We hypothesized that by physically compressing limb blood vessels, compression therapy could reduce blood flow, thereby limiting the delivery of oxaliplatin to distal nerves. This reduction in regional perfusion may, in turn, decrease peripheral drug accumulation, mitigate endoneurial edema, and reduce mechanical stress on nerve fibers—factors that collectively could attenuate neurotoxicity in the extremities.

Methods

Study design and patients

This study is a prospective, single-center, randomized controlled trial with assessor blinding. It includes colorectal cancer patients receiving their first oxaliplatin-based chemotherapy, recruited from a tertiary hospital in Nanjing between October 2023 and April 2024. Based on previous reports [3], the incidence of OIPN can be as high as 94%. In the study by Tsuyuki et al. [15], the use of one-size-smaller surgical gloves for compression therapy reduced the incidence of albumin-paclitaxel-associated sensory neuropathy by 54.7%. In this study, we aim to reduce the incidence of OIPN by approximately 35% through compression therapy. The study is designed with a two-sided α of 0.05 and a power $(1-\beta)$ of 0.9, with an equal allocation ratio of 1:1 between the intervention and control groups. According to the method proposed by Chow et al. [18], the required sample size is 27 patients per group. Considering a 20% dropout rate, a total of 66 patients (33 per group) will be enrolled. Randomization will be performed using computer-generated sequences, and allocation concealment will be achieved using opaque, sealed envelopes.

The inclusion criteria were (1) pathological confirmation of malignancy with planned oxaliplatin intravenous chemotherapy; (2) age 18–75 years; (3) Karnofsky (KPS) score ≥ 60; (4) expected survival > 3 months; and (5) informed

consent. The exclusion criteria were (1) presence of other neuropathies (e.g., severe cervical spondylosis, postherpetic neuralgia); (2) diabetic patients with peripheral sensory abnormalities; (3) patients with skin diseases or edema in the limbs; (4) chemotherapy through peripheral or PICC lines; (5) severe cardiovascular and cerebrovascular diseases, liver and kidney dysfunction; (6) pregnant or breastfeeding women; (7) patients receiving other neuroprotective drug treatments outside this trial; and (8) patients with cognitive impairments or psychiatric conditions. The termination criteria were (1) patients who change their chemotherapy regimen due to allergy or intolerance to oxaliplatin, or who discontinue chemotherapy due to disease progression, and (2) patients who switch hospitals during the observation period and are unable to continue treatment. This study has been approved by the Ethics Committee of Jiangsu Provincial Hospital of Traditional Chinese Medicine, Affiliated Hospital of Nanjing University of Chinese Medicine, China (B2021-328R) and registered with the Chinese Clinical Trial Registry (ChiCTR2300077008).

Interventions

Chemotherapy regimens ① FOLFOX regimen: oxaliplatin, 85 mg/m^2, intravenous infusion, 2–3 h, d1; calcium folinate, 400 mg/m^2, intravenous infusion, 2 h, d1; 5-FU, 400 mg/m^2, intravenous injection, d1, followed by 5-FU, 2400 mg/m^2, intravenous infusion, 46 h, d1–2. This regimen is to be repeated every 2 weeks.

② Xelox regimen: oxaliplatin, 130 mg/m^2, intravenous infusion, 2–3 h, d1; Capecitabine, 1.0–1.5 g, oral, bid, d1–14. This regimen is to be repeated every 3 weeks.

The control group received standard nursing care interventions, which included the following: (1) instructing patients to maintain warmth and avoid exposure to cold objects, metals, and cold air; (2) advising a diet that is light and devoid of spicy and irritating substances; and (3) reducing friction on the skin of the limbs and prohibiting the application of irritant liquids or ointments.

The intervention group, building on the treatment foundation of the control group, received compression therapy. This approach was informed by protocols from existing research [15, 19, 20]. On the day of each chemotherapy session, 30 min before and continuing until 30 min after the infusion of oxaliplatin, patients wore Grade II compression (23–32 mmHg) gauntlets and stockings provided by Meishuning Medical, Zhejiang Belli Medical Technology Co., Ltd. The gauntlets covered the palms and extended to just below the shoulders, while the stockings encompassed the feet, extending to just below the knees. Following the manufacturer's guidelines, researchers measured the circumferences of the wrists, the girth of the hands, the center of the palms, the ankles, and the calves to ascertain the most appropriate size of the compression garments for each patient. This intervention was administered over four chemotherapy cycles.

Outcomes

General information

The research team developed a General Information Questionnaire, which includes variables such as gender, age, cancer staging, chemotherapy regimen, and medical history. This instrument is designed to collect baseline demographic and clinical characteristics of the participants.

Primary outcome

In this study, the occurrence of OIPN was assessed using the National Cancer Institute's Common Toxicity Criteria, version 4.0 (NCI-CTCAE 4.0) [21]. The scale categorizes PN into motor and sensory neurotoxicity, which are further classified into six levels ranging from 0 to 5 based on severity. This grading standard is concise, clear, easy to manage, and widely applied in clinical settings. Research conducted by Yue [22] indicates that the scale possesses good reliability and validity. The primary endpoint of this study is the difference in the incidence rate of CTCAE ≥ 2 during treatment.

Secondary outcome

In this study, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy 20 (EORTC QLQ-CIPN20) [23] was utilized to evaluate the symptoms related to neuropathy and functional impairments in patients through self-reporting. The questionnaire comprises 20 items, including a sensory symptoms subscale with nine items (addressing tingling, numbness, pain, instability in walking or standing, and changes in temperature and hearing perception); a motor symptoms subscale with eight items (covering cramps, writing difficulties, handling small objects, and weakness); and an autonomic symptoms subscale with three items (involving vision, dizziness upon changing positions, and erectile dysfunction). All items are rated on a Likert scale of 4 levels—"none, occasional, frequent, and very frequent"—scored from 1 to 4, respectively. Scores are standardized according to the scoring instructions, with a range from 0 to 100, where higher scores indicate more severe symptoms. The EORTC QLQ-CIPN20, applicable to CIPN induced by any chemotherapy regimen, is widely used in numerous studies. Its validity and reliability have been confirmed, as well as the good internal

consistency and reliability of its subscales [24]. This scale was translated into Chinese in 2019 [25].

Safety evaluation

Adverse events were recorded through self-reporting, with patients being instructed to document any relevant adverse incidents occurring during the observation period while wearing compression sleeves and stockings, such as peripheral tingling. They were also asked to note the timing and reasons for removing the compression garments.

Given that acute OIPN symptoms typically peak within 2 to 3 days after oxaliplatin administration and may not completely resolve between treatment cycles [5, 26], neuropathy assessments were scheduled on the third day following each chemotherapy cycle to capture the maximum cumulative incidence of OIPN during the intervention phase. Two oncology attending physicians, uninvolved in randomization or treatment, independently assessed and recorded neuropathy grades using CTCAE v4.0. Under their guidance, participants completed the EORTC QLQ-CIPN20 questionnaire, which was collected only after confirming full item completion. Both assessors received pre-study training, including instruction on CTCAE v4.0 and QLQ-CIPN20 scoring criteria, case reviews, and consensus exercises to standardize interpretation. Inter-rater reliability, assessed in a random subset of evaluations, showed near-perfect agreement ($\kappa = 0.8$, $P < 0.001$), indicating excellent scoring consistency.

Statistical analysis

Statistical analyses were conducted using SPSS version 22.0. For data adhering to a normal distribution, comparisons between groups were performed using independent sample *t*-tests. For data not normally distributed, medians and interquartile ranges were used for description, and the Mann–Whitney *U* test was employed for between-group comparisons. Categorical data were expressed as frequencies and percentages, with comparisons made using the chi-square test or Fisher's exact test as appropriate. For longitudinal analysis, the study adjusted for time (as a continuous variable) and baseline values, employing mixed-effects models to analyze changes in CTCAE grades and EORTC QLQ-CIPN20 scores. All statistical tests were two-tailed, with $P < 0.05$ considered statistically significant.

All statistical analyses were conducted by the first author, who had formal training in clinical research statistics. To ensure data accuracy, two independent researchers verified all data entries and performed consistency checks. A per-protocol (PP) analysis was applied for all efficacy analyses. Missing outcome data were imputed using the last observation carried forward (LOCF) method up to the study endpoint.

Results

Patient general characteristics

This study initially recruited 66 participants, of whom 6 withdrew before completing the first two cycles of chemotherapy, leaving 60 individuals for treatment analysis (Fig. 1). A comparison of general characteristics between the two groups revealed no statistically significant differences ($P > 0.05$), as shown in Table 1.

Primary outcome measure

The comparison results of the incidence rates of sensory and motor PN (CTCAE grade ≥ 2) between the two groups are shown in Table 2. After the completion of the first two chemotherapy cycles, there was no statistically significant difference in the incidence of sensory and motor PN between the groups, with $P > 0.05$. However, by the end of the third chemotherapy cycle, the incidence of sensory neuropathy in the compression therapy group was lower than that in the control group (31.0% vs. 58.1%, $P = 0.035$). Although there was still no statistically significant difference in the incidence of motor neuropathy between the groups (24.1% vs. 48.4%, $P = 0.051$), a trend toward reduction was evident. After the fourth chemotherapy cycle, statistically significant differences were observed in the incidence of both sensory and motor PN between the groups, with $P < 0.05$.

In the longitudinal analysis, the model results indicate that with an increase in cycles of oxaliplatin chemotherapy, there was a rising trend in the incidence of both sensory and motor PN in the two groups (sensory: OR = 3.611, 95% CI [2.470, 5.280], $P < 0.001$; motor: OR = 3.381, 95% CI [2.276, 5.022], $P < 0.001$). The difference in trends between the two groups was statistically significant (sensory: OR = 0.294, 95% CI [0.139, 0.625], $P = 0.001$; motor: OR = 0.265, 95% CI [0.119, 0.590], $P = 0.001$) (Table 4), suggesting that compression therapy may attenuate the development and progression of OIPN.

Secondary outcome measures

Comparisons of the EORTC QLQ-CIPN20 scores after each chemotherapy cycle shown in Table 3. Following the third chemotherapy cycle, the difference in scores between the groups began to reach statistical significance ($Z = -2.918$, $P = 0.004$). Longitudinal analysis indicated that with the increase in cumulative doses of oxaliplatin, EORTC QLQ-CIPN20 scores increased ($\beta = 4.141$, 95%

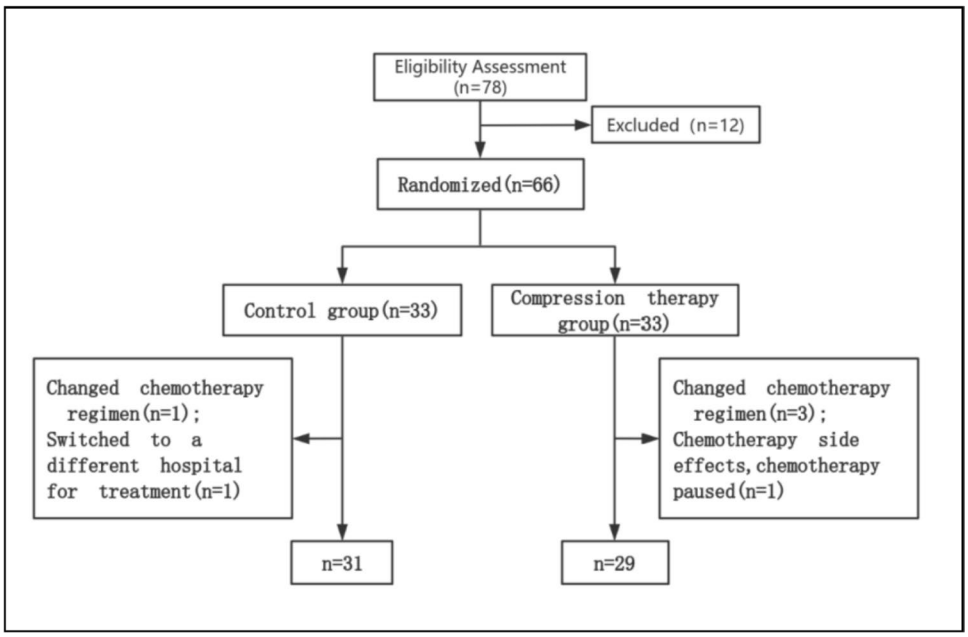

Fig. 1 Flow diagram of the study

Table 1 Demographics and clinical characteristics of participants

Characteristics	Control ($n = 31$)	Compression therapy ($n = 29$)	T/χ^2	P
Age (mean ± SD)	60.68 ± 9.40	58.07 ± 8.28	1.137	0.260
BMI (kg/m^2)	23.71 ± 3.55	23.65 ± 3.31	0.061	0.951
Gender (n, %)			0.352	0.553
Male	18 (58.1)	19 (65.5)		
Female	13 (41.9)	10 (34.5)		
Tumor stage (n, %)			1.153	0.640
II	8 (25.8)	5 (17.2)		
III	20 (64.5)	19 (65.5)		
IV	3 (9.7)	5 (17.3)		
Chemotherapy regimen (n, %)			2.550	0.110
FOLFOX	20 (64.5)	24 (82.8)		
XELOX	11 (35.5)	5 (17.2)		
Diabetic (n, %)	4 (12.9)	3 (11.7)	0.000	1.000
Drinking (n, %)	2 (6.5)	2 (6.9)	0.000	1.000
Smoking (n, %)	1 (3.2)	3 (10.3)	0.344	0.557

Table 2 Comparison of peripheral neuropathy incidence rates between the two groups across different chemotherapy cycles (CTCAE ≥ 2) (n, %)

	Cycle	**Control ($n = 31$)**	**Compression therapy ($n = 29$)**	**χ^2**	***P***	**Rate difference 95% CI**
Sensory	1	2 (6.5%)	1 (3.4%)	0.285	0.594	0.140 to − 0.078
	2	10 (32.3%)	5 (17.2%)	1.802	0.179	0.365 to − 0.063
	3	18 (58.1%)	9 (31.0%)	4.423	0.035*	0.513–0.029
	4	25 (80.6%)	12 (41.4%)	9.773	0.002*	0.619–0.165
Motor	1	2 (6.5%)	0 (0%)	0.451	0.502	0.152 to − 0.022
	2	9 (29.0%)	4 (13.8%)	2.050	0.152	0.355 to − 0.051
	3	15 (48.4%)	7 (24.1%)	3.794	0.051	0.478–0.080
	4	21 (67.7%)	10 (34.5%)	6.637	0.010*	0.571–0.093

*$P < 0.05$

Table 3 Comparison of EORTC QLQ-CIPN20 scores between the two groups of participants across different chemotherapy cycles [score, *M* (P25, P75)]

Cycles	Control ($n = 31$)	Compression therapy ($n = 29$)	Z	P
1	25.0 (25.0, 27.8)	25.0 (25.0, 25.7)	− 1.474	0.141
2	30.6 (25.0, 35.0)	28.9 (25.0, 31.6)	− 1.690	0.091
3	36.3 (32.5, 39.5)	32.5 (30.8, 35.1)	− 2.918	0.004*
4	41.3 (37.5, 43.4)	34.7 (32.5, 38.5)	− 4.028	< 0.001*

*$P < 0.05$

CI = [3.77, 4.513], $P < 0.001$). However, the application of compression therapy significantly mitigated the upward trend in EORTC QLQ-CIPN20 scores ($\beta = -2.157$, 95% CI = [− 3.050, − 1.264], $P < 0.001$) (Table 4).

Safety

All patients in the compression therapy group demonstrated good tolerance to the compression sleeves and stockings, completing the therapy as required. Furthermore, there were no adverse events associated with the use of compression sleeves and stockings.

Discussion

CIPN is a common adverse reaction to anticancer drugs. A systematic review and meta-analysis involving over 4000 chemotherapy patients reported a CIPN prevalence of 68.1% in the first month of chemotherapy [27]. Clinically, CIPN presents as sensory and motor abnormalities, typically initially affecting the lower limbs and, in severe cases, extending to the proximal regions of all four limbs [28]. This can lead to physical dysfunction, increased risk of falls, and decreased quality of life for the patient [9], potentially resulting in delayed chemotherapy, reduced dosage, or even premature termination of treatment [29]. However, current evidence-based pharmacological treatments for CIPN are limited, with no clear preventive recommendations. Various studies, both domestically and internationally, have explored external treatment methods. Cryotherapy has shown promise in preventing CIPN, but its clinical application is limited due to poor tolerance and high dropout rates among patients, preventing its widespread recommendation in clinical practice [8]. Japanese scholars, drawing on the mechanism of action of cryotherapy, have adopted compression therapy as an alternative method for the prevention of CIPN, attracting widespread attention. Tsuyuki [15] conducted a study with 42 breast cancer patients undergoing chemotherapy with albumin-bound paclitaxel. Using a self-control method, patients wore two layers of surgical gloves that were one size smaller on the dominant hand from 30 min before to 30 min after chemotherapy administration. The results showed significant reductions in sensory and motor PN on the glove-wearing side (sensory neuropathy: 21.4% vs. 76.1%; motor neuropathy: 26.2% vs. 57.1%). Kanbayashi [30] compared cryotherapy and compression therapy in patients undergoing paclitaxel chemotherapy, finding that both methods were similarly effective. Accordino et al.'s study [20] compared the efficacy and tolerability of cryotherapy, compression therapy, and placebo in preventing CIPN during taxane chemotherapy. The results demonstrated that compression therapy was the most effective and well tolerated. Recent RCTs [31, 32] also support the effectiveness of compression therapy in significantly reducing the incidence of CIPN. However, most subjects in compression therapy studies have been breast or gynecologic cancer patients undergoing paclitaxel or docetaxel chemotherapy, which may introduce gender-related biases. Oxaliplatin (L-OHP) is considered one of the most neurotoxic chemotherapeutic agents, with nearly 90% of patients experiencing acute and transient neuropathy, often exacerbated by cold exposure [33]. Consequently, the "Expert consensus on the prevention and treatment of chemotherapy-induced peripheral neuropathy by integrated Chinese and Western medicine" does not recommend cryotherapy for preventing OIPN [34]. Given that colorectal cancer is the second leading cause of cancer death worldwide [35], and L-OHP is a primary chemotherapy or adjuvant

Table 4 Mixed model (logit) analysis of CTCAE grading and EORTC QLQ-CIPN20 scores with baseline adjustment

	Compression therapy			**Chemotherapy cycles (T)**		
	OR/β	***P***	**95% CI**	***OR/β***	***P***	**95% CI**
CTCAE (≥ grade 2)						
Sensory	0.294	0.001*	0.139–0.625	3.611	< 0.001*	2.470–5.280
Motor	0.265	0.001*	0.119–0.590	3.381	< 0.001*	2.276–5.022
CIPN20	− 2.157	< 0.001*	− 3.050 to − 1.264	4.141	< 0.001*	3.77–4.513

For CTCAE, $OR < 1$ indicates a lower likelihood of neuropathy occurrence; $OR > 1$ indicates a higher likelihood of neuropathy occurrence.

For EORTC QLQ-CIPN scores, $\beta < 0$ indicates lower scores; $\beta > 0$ indicates higher scores.

*$P < 0.05$.

treatment for colorectal cancer patients [36], exploring effective methods to prevent OIPN is crucial. This study utilized a randomized controlled trial to apply compression therapy to colorectal cancer patients undergoing L-OHP chemotherapy, aiming to produce high-quality evidence.

A previous study reported that the use of small-sized surgical gloves could lead to patient discomfort [37], and current compression therapy primarily targets the upper limbs, lacking preventive effects for the lower limbs. A RCT comparing compression therapy and cryotherapy interventions for CIPN, conducted by Columbia University in the USA, involved patients wearing 20–30 mmHg compression gloves and socks during chemotherapy infusion [20]. Therefore, in this study, to prevent OIPN, participants wore grade II (23–32 mmHg) compression sleeves and stockings on both hands and feet. Effectiveness was evaluated through a combination of physician assessments and self-reports. Based on the results of the CTCAE grading and CIPN20 scores, from the third cycle of L-OHP chemotherapy, the incidence of sensory neuropathy in the compression therapy group was significantly lower than that in the control group, and patients in the compression therapy group also experienced a lower burden of peripheral neuropathy symptoms. After the fourth chemotherapy cycle, the total incidence of sensory neuropathy of CTCAE ≥ 2 in the compression therapy group was reduced to 41.4% (control is 80.6%). Moreover, the incidence of motor neuropathy in the compression therapy group was also significantly lower than that in the control group, with statistical significance. The results of the longitudinal analysis indicate that as chemotherapy cycles increased and the cumulative dose of L-OHP rose, both groups experienced an increase in the incidence and symptom burden of sensory and motor neuropathy. However, compression therapy was able to reduce this rising trend and slow the progression of OIPN, suggesting that compression therapy is effective in preventing OIPN. It also alleviates neuropathy-related symptoms, improving patients' quality of life. As illustrated in Fig. 2, external limb compression during oxaliplatin administration reduces blood flow to the limbs and thereby shields peripheral nerves from high drug concentrations, which potentially prevents neuropathic symptoms. This hypothesized mechanism provides a rationale for the neuroprotective effect of compression therapy in OIPN prevention and is supported by our implementation of the technique in the study. But recent studies have shown that compression therapy using surgical gloves does not prevent PN induced by paclitaxel (PTX) [38] or vincristine (VCR) [39]. The differing results may be attributed to the varying incidence rates of PN associated with PTX, VCR, and L-OHP. Additionally, the study populations differed, with one focusing on breast cancer patients and the other on malignant lymphoma patients, which may have also influenced the outcomes. Finally, differences in study design may

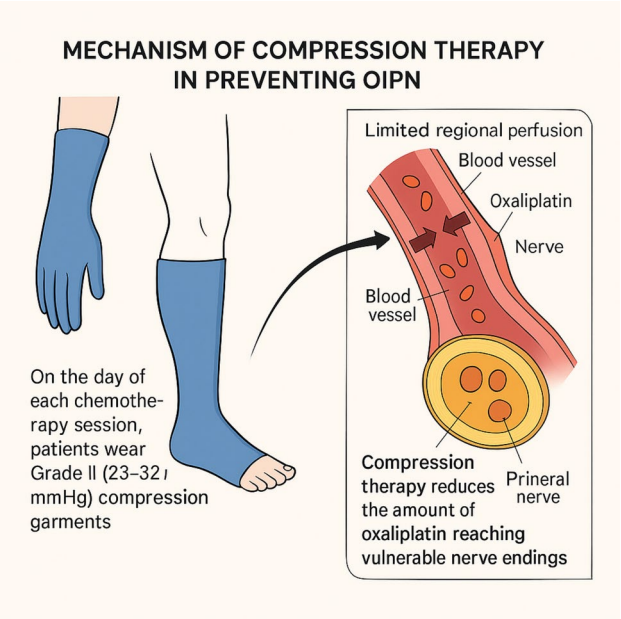

Fig. 2 Mechanism of compression therapy in preventing OIPN

also be one of the reasons for the different results observed. Both studies employed a self-controlled design, using surgical gloves to apply pressure to one hand.

In this study, patients in the compression therapy group were required to wear compression sleeves and stockings for a total of approximately 4 h before and after the infusion of L-OHP. We allowed patients to intermittently remove the compression garments as needed to enhance tolerability, but the frequency and duration of removals were documented. Aside from those who changed chemotherapy regimens or terminated treatment, all participants in our study completed the research without discontinuing the use of compression sleeves and stockings due to intolerance. Furthermore, there were no adverse events related to compression therapy, such as skin itching or erythema, reported. These results suggest that compression therapy with sleeves and stockings is safe for preventing OIPN, with high patient compliance.

This study has certain limitations. First, although the compression devices and methods used in our study are affordable and easy to replicate, the applied pressure could not be objectively measured. Future studies could employ pressure measurement instruments to apply varying pressure levels to the limbs of patients undergoing oxaliplatin chemotherapy, to observe preventative effects and identify optimal pressure values. Second, due to the inherent nature of compression therapy, blinding was not implemented for researchers and participants, which may introduce reporting bias. Third, there is a lack of objective methods to assess neuropathy. Currently, there are no standardized objective tools for the assessment and diagnosis of CIPN. Some

studies have employed neurophysiological tests [40], including nerve conduction studies (NCS) and electromyography (EMG). However, these methods primarily evaluate large myelinated fiber pathology, whereas CIPN preferentially damages small fibers, and these approaches are both costly and time-consuming. In this study, the CTCAE 4.0 was assessed and graded by healthcare professionals, and the EORTC QLQ-CIPN20 questionnaire was a self-report scale completed by patients based on symptoms experienced in the previous week. Discrepancies between some patients' CIPN20 scores and physicians' CTCAE grades highlight the limitations of using subjective methods to evaluate P. Fourth, this study is that neuropathy was not assessed beyond the four-cycle intervention period, precluding evaluation of long-term chronic OIPN progression or the coasting phenomenon, which may occur after treatment discontinuation. Additionally, because this study focused on the overall incidence of OIPN, without distinguishing between acute and chronic forms, the findings should be interpreted accordingly. Future studies with extended follow-up are needed to determine the long-term protective effects of compression therapy on chronic neurotoxicity. Fifth, we did not monitor limb temperature during the compression therapy period. As compression therapy primarily reduces blood flow through mechanical pressure rather than temperature modulation, limb temperature measurements were not included in the study protocol. Nonetheless, the absence of temperature and perfusion data precludes the exclusion of potential secondary thermal or physiological effects. Future studies should incorporate objective physiological assessments, such as continuous limb temperature and perfusion monitoring, to better characterize the vascular effects of compression therapy and elucidate their relationship with clinical outcomes.

Conclusion

This study demonstrated that implementing compression therapy in colorectal cancer patients undergoing oxaliplatin chemotherapy effectively reduced the incidence of sensory and motor PN, slowed the progression of OIPN, and alleviated OIPN-related symptom burden. This finding provides a feasible intervention for clinical oncology practice, potentially reducing the risk of neurotoxicity associated with oxaliplatin chemotherapy. However, the study has some limitations, including the lack of blinding, a short intervention and observation period of only four chemotherapy cycles, the absence of objective measurement indicators, the lack of long-term follow-up, and the inability to assess the development or persistence of chronic OIPN. Therefore, these results require further validation. Future research should involve more rigorous, multicenter, large-sample prospective randomized controlled trials to establish effective methods for preventing oxaliplatin-induced peripheral neuropathy in clinical settings.

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Author contributions ZXT and YL made significant contributions to the design of the study and drafted the manuscript; YL and LJW made substantial contributions to data collection, entry, and analysis; YY and GYY played significant roles in the implementation of the protocol; LWZ and SJ were responsible for the assessment of CTCAE grading and clinical evaluation; SZL rigorously reviewed the manuscript and supervised the entire research process. All authors have read and approved the final manuscript.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki, and has been approved by the Ethics Committee of Jiangsu Provincial Hospital of Traditional Chinese Medicine, Affiliated Hospital of Nanjing University of Chinese Medicine, China (B2021-328R).

Consent to participate Informed consent was obtained from all participants in this study.

Consent for publication This study did not include any personal data.

Competing interests The authors declare no competing interests.

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