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A Noninvasive Acupoint Patch as an Adjunct to Antiemetic Therapy for Chemotherapy-Induced Nausea and Vomiting: A Multicenter Randomized Crossover Trial

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Abstract

Purpose

Chemotherapy-induced nausea and vomiting (CINV) remains an important chemotherapy-related toxicity in patients receiving moderately emetogenic chemotherapy (MEC), despite standard antiemetic prophylaxis. This study evaluated the efficacy and safety of a noninvasive acupoint patch, the Novel Jiangni Zhitu Patch (N-JZP), as an adjunct to standard dual antiemetic therapy for preventing CINV.

Methods

This multicenter, randomized, double-blind, sham-controlled crossover trial enrolled 96 patients with malignant tumors scheduled to receive MEC. Participants were assigned 1:1 to two treatment sequences across two consecutive chemotherapy cycles. In one cycle, participants received standard dual antiemetic therapy plus N-JZP applied to PC6, ST36, and CV8; in the other cycle, they received standard therapy plus a visually identical sham patch. The primary outcome was Grade ≥ 2 CINV during the chemotherapy cycle, assessed at day 3 and day 7.

Results

Ninety-six patients were included in the intention-to-treat analysis and 68 in the per-protocol analysis. Grade ≥ 2 CINV occurred in 26.0% of cycles during N-JZP exposure and 42.7% during sham exposure. N-JZP significantly reduced Grade ≥ 2 CINV after adjustment using generalized estimating equations (OR 0.47, 95% CI 0.25–0.87; P = 0.017), with a number needed to treat of approximately 6. Per-protocol findings were consistent (25.0% vs. 47.1%; OR 0.38; P = 0.003). Local skin reactions were uncommon and identical between groups (1.1%).

Conclusion

N-JZP added to standard dual antiemetic therapy reduced moderate-to-severe CINV with minimal local toxicity, supporting its potential role as a low-burden adjunctive supportive-care intervention.

Trial registration

http//itmctr.ccebtcm.org.cn/ (Registration No. ITMCTR2024000624).

Key Message

This multicenter crossover trial found that a noninvasive acupoint patch added to dual antiemetic therapy reduced moderate-to-severe CINV in patients receiving MEC, with an NNT of approximately 6 and minimal local toxicity.

Introduction

CINV remains one of the most common and distressing adverse effects experienced by patients receiving systemic anticancer therapy. It can impair nutritional intake, disrupt daily functioning, reduce quality of life, and compromise adherence to planned chemotherapy schedules [1]. International guidelines, including those from the National Comprehensive Cancer Network (NCCN) and the Multinational Association of Supportive Care in Cancer/European Society for Medical Oncology (MASCC/ESMO) [2], universally position pharmacological prophylaxis as the core strategy for CINV management. However, despite the recommendation of various antiemetic regimens, a substantial proportion of patients receiving MEC fail to achieve complete protection, particularly in the delayed phase [3].

Pharmacologic prophylaxis remains the cornerstone of CINV management. However, escalation of antiemetic treatment may increase pill burden, cost, and adverse effects, and may not fully address delayed or persistent nausea. Therefore, low-burden adjunctive interventions that can be integrated into routine chemotherapy care without adding substantial systemic medication exposure are clinically relevant. Acupoint patch therapy in Traditional Chinese Medicine (TCM) is a non-invasive intervention that combines acupoint stimulation with the transdermal delivery of herbal constituents [4]. It possesses a strong theoretical foundation and historical application in alleviating gastrointestinal discomfort [5]. Drawing on long-term clinical practice and classical TCM prescriptions, our team developed a herbal formulation for nausea and vomiting associated with cancer-related complications [6], obtaining a Chinese invention patent in 2017 (Patent No. CN104189792B; ZL201410350685.2) [7]. Building on this, we further optimized the dosage form into a gel-based herbal acupoint patch to improve stability and transdermal delivery.

However, existing clinical studies evaluating herbal acupoint patches for CINV have often been limited by small sample sizes, suboptimal blinding, and parallel designs that fail to fully account for inter-individual variability [8,9]. Therefore, we conducted a multicenter, randomized, double-blind, placebo-controlled crossover trial to evaluate the efficacy and safety of N-JZP, combined with standard dual antiemetic therapy, in patients undergoing MEC. Although triple antiemetic therapy is currently recommended as a first-line option, dual therapy remains a standard alternative for patients receiving MEC, according to both international and Chinese clinical guidelines [2,10,11]. In real-world practice, dual antiemetic prophylaxis continues to be frequently utilized for MEC. Furthermore, employing a dual-regimen baseline allows for the precise isolation of the independent net clinical benefit of N-JZP, providing direct, translatable evidence for an integrative combination approach [1].

Methods

Study design

This was a prospective, randomized, double-blind, placebo-controlled crossover clinical trial. The study was conducted across five hospitals in North China between November 2024 and July 2025, led by Beijing Hospital of Traditional Chinese Medicine, Capital Medical University. Other participating centers included Shunyi Hospital of Beijing Hospital of Traditional Chinese Medicine, The First Affiliated Hospital of Hebei North University, Weifang Hospital of Traditional Chinese Medicine, and Jiaozuo Second People's Hospital. Participants were randomly assigned in a 1:1 ratio to either Sequence A or Sequence B. Sequence A received standard antiemetic therapy plus the true acupoint patch in Cycle 1, followed by standard therapy plus the sham patch in Cycle 2. Sequence B received the interventions in the reverse order. The study protocol was approved by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine (Approval No. 2024BL02-026) and strictly adhered to the Consolidated Standards of Reporting Trials (CONSORT) statement and its extension for crossover trials [12,13].

Participants

Eligible participants were adults aged 18 to 75 years with a histologically confirmed malignancy, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 3, and an expected survival of >3 months, who were scheduled to receive at least two consecutive cycles of intravenously administered MEC. MEC regimens included irinotecan, carboplatin, nedaplatin, lobaplatin, oxaliplatin, or anthracycline-based therapies (doxorubicin ≤ 60 mg/m² or epirubicin ≤ 90 mg/m²). Participants were either chemotherapy-naïve or had a chemotherapy-free interval of at least one month prior to enrollment.

The definition and management of CINV adhered to the guidelines of the Chinese Pharmacists Association (T/CPHARMA 006-2021). CINV severity was assessed using the World Health Organization (WHO) toxicity grading criteria for acute and subacute reactions to anticancer drugs: grade 0 (none), grade I (nausea), grade II (transient vomiting), grade III (vomiting requiring therapy), and grade IV (intractable vomiting).

Key exclusion criteria included the following: planned radiotherapy for isolated brain, bone, or adrenal metastases; concomitant use of two or more non-chemotherapy antitumor drugs; other known causes of nausea or vomiting; severe cardiac, hepatic, renal, hematologic, or endocrine disorders; pregnancy or breastfeeding; known allergies to the study materials; or concurrent participation in another clinical trial. To enhance feasibility and generalizability, participants receiving chemotherapy combined with a single targeted agent or an immune checkpoint inhibitor were permitted to enroll; however, those receiving two or more such agents concurrently were excluded to limit clinical heterogeneity.

Randomization and blinding

Participants were randomly assigned in a 1:1 ratio to either Sequence A or Sequence B (Fig. 1), utilizing a block randomization list (block size of 4) generated by an independent statistician. Allocation concealment was strictly maintained using sequentially numbered, sealed, and opaque envelopes. A double-blind design was implemented, ensuring that participants, clinicians, outcome assessors, and statisticians remained blinded to the treatment assignments. The active and sham patches were completely indistinguishable in terms of appearance, odor, and texture. To further ensure blinding during the trial, patch packages were simply coded as V1 and V2 (corresponding to cycle 1 and cycle 2) and labeled with the respective participant identification numbers (1–96).

Interventions

Study patches: N-JZP contained a patented herbal formula composed of processed Pinellia ternata (Jiang Banxia), Aucklandia lappa (Muxiang), and dried Zingiber officinale (Ganjiang). The formulation was optimized into a gel-based matrix using an improved volatile-oil extraction procedure and subsequent integration into a sodium polyacrylate gel substrate. In an in vitro permeation experiment, the optimized gel matrix increased the mean transdermal permeation rate of 6-gingerol by 1.53-fold compared with the original paste formulation. Quality evaluation adhered to the Chinese Pharmacopoeia standards for topical plasters (including content and adhesion assessments) [14], and thin-layer chromatography was utilized for constituent identification. The sham patch was completely identical in appearance, odor, and texture, but devoid of any active herbal ingredients.

Patch application: The patches were applied to the bilateral Neiguan (PC6) and Zusanli (ST36) acupoints, as well as the Shenque (CV8) acupoint, once daily for 6 hours. This regimen commenced on day 1 of chemotherapy and continued for 5 consecutive days. Participants documented their adherence in a daily diary. The use of other TCM decoctions or proprietary TCM products intended to alleviate nausea and vomiting was strictly prohibited during the intervention period.

Background antiemetic prophylaxis: All participants received a standard dual antiemetic therapy consisting of a 5-hydroxytryptamine type 3 ($5\text{-}HT_3$) receptor antagonist ($5\text{-}HT_3RA$) plus dexamethasone on days 1 to 3 of the chemotherapy cycle. This protocol is consistent with both the NCCN antiemesis guidelines [15] and the Chinese guidelines [10]. To prevent confounding, the antiemetic regimen was kept strictly consistent for each participant across both crossover cycles.

Outcomes

Follow-up assessments were conducted on day 3 and day 7 post-chemotherapy, deviating from the traditional segmented observation windows of acute (0–24 h) and delayed (24–120 h) phases [16]. Because delayed CINV typically peaks between 48 and 72 hours and may persist for approximately 6 to 7 days [17,18], the day 3 assessment captures the anticipated peak period, whereas the day 7 assessment provides an extended window for observing delayed symptoms.

Primary outcome: The primary outcome was the proportion of participants experiencing Grade ≥ 2 CINV during the entire chemotherapy cycle, based on the WHO toxicity grading recorded at the day 3 and day 7 assessments.

Secondary outcomes: Secondary outcomes included: (1) the proportion of participants with any-grade (Grade ≥ 1) CINV over the cycle (the inverse of which corresponds to complete protection); (2) the incidence of Grade ≥ 2 CINV specifically at day 3 and day 7; (3) scores from the Functional Living Index–Emesis (FLIE) questionnaire; and (4) quality of life assessed via the EQ-5D. Adverse events other than nausea and vomiting were evaluated using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, with a specific focus on monitoring local skin reactions.

Sample size

Sample size estimation was based on previous data from our team, which suggested that the incidence of Grade ≥ 2 CINV could decrease from 53.3% to 23.3% [6]. Although crossover designs inherently reduce between-participant variability, the primary endpoint was binary; therefore, a two-proportion comparison model was utilized (two-sided $\alpha = 0.05$, power = 0.80). Using PASS 15.0 software, the minimum sample size was calculated to be 76 participants. Assuming a 20% attrition rate, a total of 96 participants (48 per sequence) were targeted for enrollment.

Statistical analysis

Statistical analyses were performed using R software (version 4.5.1) [19]. The primary analysis was conducted on the intention-to-treat (ITT) set, whereas participants who completed both crossover periods constituted the per-protocol (PP) set. Missing outcome data at day 3 and day 7 were addressed using multiple imputation by chained equations (MICE) [20] via logistic regression, under the missing-at-random assumption. Binary endpoints were analyzed using generalized estimating equations (GEE) with a logit link function, adjusting for period effects, sequence effects, and baseline covariates. To ensure the robustness of the findings, sensitivity analyses were performed using generalized linear mixed models (GLMM). Continuous outcomes were analyzed using linear mixed-effects models. All statistical tests were two-sided, with $P < 0.05$ considered to indicate statistical significance. Effect sizes are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Results

Participant flow and attrition

A total of 96 participants were randomized and included in the intention-to-treat (ITT) set (Fig. 2). During the study, 28 participants discontinued, resulting in an overall dropout rate of 29.2% (28/96). The majority of these discontinuations occurred prior to the second crossover period. Primary reasons for

withdrawal included refusal to continue the second-stage patching or chemotherapy, changes in treatment regimens, and clinical deterioration that precluded further participation. Notably, only one participant withdrew due to a mild skin rash. No clustered dropouts related to serious adverse events or safety concerns were observed. Furthermore, participant dropout was not significantly associated with the occurrence of Grade ≥ 2 CINV (P = 0.35). This suggests that attrition was unlikely to be driven by more severe symptoms or to introduce systematic bias related to the intervention.

Baseline characteristics

Baseline characteristics were comparable between the per-protocol (PP) population and the dropout group, with no significant differences observed in sex, age distribution, ECOG performance status, education level, metastatic status, or prior chemotherapy exposure (all P > 0.05). Participants aged ≥ 50 years accounted for more than 90% of both groups, demonstrating a highly consistent age distribution. Although the proportion of patients with metastasis was numerically higher in the dropout group compared to the PP population (82.1% vs. 66.2%), this difference did not reach statistical significance (P = 0.143). This numerical trend is clinically plausible, as patients with more advanced disease are generally more likely to discontinue participation during multi-cycle crossover trials.

The baseline characteristics of the PP set are summarized in Table 1. The two randomization sequences were well-balanced and comparable across all recorded variables. Within the ITT set, 13 of the 96 participants (13.5%) received chemotherapy combined with a single targeted agent or immune checkpoint inhibitor; in the PP set, this proportion was 12 of 68 participants (17.6%).

Table 1
Baseline Demographic and Clinical Characteristics (PP Set)

Variable		Group A	Group B	Total	Statistic	P-value
		(n = 31)	(n = 37)	(N = 68, 100%)		
Age (Mean ± SD)		64.13 ± 10.01	63.65 ± 9.54	63.87 ± 9.69	0.202	> 0.05
Gender	Male	18	17	35 (51.5%)	0.992	> 0.05
	Female	13	20	33 (48.5%)		
ECOG PS	0	13	12	25 (36.7%)	0.655	> 0.05
	1	13	18	31 (45.5%)		
	2	5	7	12 (17.6%)		
BMI	Underweight (< 18.5)	0	4	4 (5.9%)	4.082	> 0.05
	Normal (18.5–23.9)	18	19	37 (54.4%)		
	Overweight (24.0–27.9)	10	9	19 (27.9%)		
	Obese (≥ 28.0)	3	5	8 (11.8%)		
Education	Illiterate	1	0	1 (1.5%)	3.656	> 0.05
	Primary school	9	17	26 (38.2%)		
	Middle/High school	17	18	35 (51.5%)		
	University/College	4	2	6 (8.8%)		
Metastasis	Yes	17	28	45 (66.2%)	3.272	> 0.05
	No	14	9	23 (33.8%)		
First-time Chemo	Yes	23	30	53 (77.9%)	0.465	> 0.05
	No	8	7	15 (21.1%)		

Primary outcome

In the ITT set, the incidence of Grade ≥ 2 CINV was 26.0% (25/96) during the active patch period compared with 42.7% (41/96) during the sham patch period (absolute risk reduction [ARR] = 16.7%; NNT ≈ 6). After adjusting for confounding factors using the GEE model, the active patch significantly reduced the risk of Grade ≥ 2 CINV (OR = 0.47, 95% CI: 0.25–0.87; P = 0.017;Fig. 3, Table 2). Consistent results

were observed in the PP set, with incidences of 25.0% (17/68) versus 47.1% (32/68) (ARR = 22.1%; NNT ≈ 5) and a highly significant adjusted effect (OR = 0.38, 95% CI: 0.20–0.72; P = 0.003). Robustness analyses utilizing GLMMs yielded consistent findings (ITT: OR = 0.38, P = 0.004; PP: OR = 0.36, P = 0.007;Fig. 3, Table 2). Furthermore, no statistically significant period or sequence effects were detected (P > 0.05).

Secondary outcomes

In the PP set, the incidence of any-grade (Grade ≥ 1) CINV was 72.1% (49/68) during the active patch period compared with 86.8% (59/68) during the sham patch period (OR = 0.36, 95% CI: 0.14–0.92; P = 0.034), as shown in Fig. 4 and Table 2. In time-specific adjusted analyses, the active patch significantly reduced the risk of Grade ≥ 2 CINV at both day 3 (OR = 0.393, 95% CI: 0.158–0.974; P = 0.044) and day 7 (OR = 0.442, 95% CI: 0.201–0.973; P = 0.042), as shown in Table 3. No statistically significant differences were observed between the two groups regarding nausea and vomiting visual analog scale (VAS) scores or EQ-5D scores (all P > 0.05).

Table 2
Comparison of Primary and Secondary Efficacy Outcomes

Outcome	True Patch Group	Sham Patch Group	Absolute Risk Reduction (ARR)	GEE-Adjusted OR (95% CI)	*P*-value
Primary Outcome (Grade ≥ 2 CINV)					
ITT Set (n = 96)	25 (26.0%)	41 (42.7%)	16.7%	0.47 (0.25–0.87)	0.017
PP Set (n = 68)	17 (25.0%)	32 (47.1%)	22.1%	0.38 (0.20–0.72)	0.003
Secondary Outcome (Grade ≥ 1 CINV)					
PP Set (n = 68)	49 (72.1%)	59 (86.8%)	14.7%	0.36 (0.14–0.92)	0.034

Table 3
Multivariate GEE Analysis for Risk of Grade ≥ 2 CINV

Variable	OR		95% CI Lower		95% CI Upper		*P*-value	
	D3	D7	D3	D7	D3	D7	D3	D7
True patch vs Sham	0.393	0.442	0.158	0.201	0.974	0.973	0.044	0.042
Period (Cycle 2 vs 1)	1.100	0.616	0.445	0.279	2.710	1.360	0.839	0.229
Sequence (B vs A)	2.010	0.898	0.803	0.400	5.050	2.020	0.136	0.793
Sex (Male vs Female)	0.596	1.940	0.248	0.859	1.430	4.400	0.248	0.111
Age (≥ 50 vs < 50)	0.957	0.577	0.244	0.144	3.760	2.310	0.950	0.437
ECOG 1 vs 0	1.210	1.580	0.443	0.629	3.300	3.980	0.711	0.330
ECOG 2 vs 0	2.190	2.810	0.640	0.874	7.510	9.010	0.211	0.083
First-time Chemo (Yes vs No)	0.779	0.857	0.307	0.323	1.980	2.280	0.599	0.757
Metastasis (Yes vs No)	1.420	1.140	0.527	0.481	3.820	2.680	0.490	0.772

Safety

Local skin reactions (e.g., erythema or pruritus) were rare and comparable between the two treatment groups (1.1% [1/95] in each group). No patch-related serious adverse events occurred during the study. The use of rescue antiemetics beyond the protocol-specified dual regimen did not differ significantly between the treatments (active patch: 4.2% [4/95] vs. sham patch: 10.5% [10/95]; P > 0.05, Table 4). Across all standardized observation periods, rescue antiemetics were utilized in 14 of 190 periods (7.4%), with no statistically significant difference between the active and sham interventions (P > 0.05).

Table 4
Concomitant Medication (Rescue Antiemetics)

Treatment Group	Use of Rescue Antiemetics, n (%)
True Patch	4/95 (4.2%)
Sham Patch	10/95 (10.5%)

Discussion

This multicenter, randomized, double-blind, sham-controlled crossover trial demonstrated that N-JZP, when added to standard dual antiemetic therapy, significantly reduced moderate-to-severe CINV in patients receiving MEC. The absolute reduction of 16.7% in the ITT analysis and 22.1% in the PP analysis suggests a clinically meaningful adjunctive benefit. Importantly, this benefit was achieved without an

increase in local skin reactions or rescue antiemetic use, supporting the feasibility of N-JZP as a low-burden supportive-care intervention for chemotherapy-related toxicity.

In this study, conducted across five hospitals in North China, N-JZP used alongside standard dual antiemetic prophylaxis significantly reduced the risk of moderate-to-severe CINV. Local skin reactions were rare and identical under both conditions. The magnitude of benefit observed in this trial is relevant from a supportive oncology perspective. CINV is not only a treatment-related adverse event but also a symptom burden that affects nutrition, daily functioning, sleep, emotional well-being, and willingness to continue chemotherapy. Although guideline-based antiemetic prophylaxis remains essential, a substantial proportion of patients continue to experience nausea and vomiting despite standard regimens. A noninvasive adjunctive intervention that can be added to usual care with minimal systemic exposure and low local toxicity may therefore have practical value, particularly for patients who prefer to avoid additional medications or who are vulnerable to adverse effects from systemic antiemetics.

Several methodological features strengthen the internal validity and clinical relevance of this study. The randomized crossover structure ensured that each participant served as their own control, minimizing inter-individual confounding by stable characteristics that influence nausea susceptibility but are difficult to measure in oncology populations. Strict double-blinding and a sensory-matched sham patch effectively reduced expectancy and performance biases. Analytically, ITT principles were paired with MICE for missing outcomes, GEE for correlated crossover data, and GLMM robustness analyses, providing convergent support for the primary inference.

This trial also provides a pragmatic example of modernizing and standardizing a TCM external therapy. The patented herbal formula was incorporated into a gel-based matrix and evaluated according to Chinese Pharmacopoeia standards. In an *in vitro* permeation experiment, the optimized gel matrix increased the transdermal permeation rate of 6-gingerol by 1.53-fold compared with the original paste formulation, supporting enhanced drug delivery while maintaining excellent skin tolerability.

The observed antiemetic benefit is biologically plausible and likely reflects synergy between acupoint stimulation and the transdermal delivery of multiple herbal constituents [4]. From a TCM perspective, chemotherapy may impair spleen-stomach function and disrupt qi regulation, leading to “rebellious” stomach qi and nausea/vomiting [21]; the formula (processed Pinellia ternata, Aucklandia lappa, and dried Zingiber officinale) aligns with harmonizing the stomach and descending counterflow. The selected acupoints—Neiguan (PC6), Zusanli (ST36), and Shenque (CV8)—are frequently identified in evidence syntheses and acupoint-selection analyses for CINV [5]. From a biomedical standpoint, emesis involves a gut-brain axis with key roles for 5-HT and substance P, particularly in delayed symptoms. Improved 6-gingerol delivery may contribute via the modulation of emesis-related pathways [22, 23], while acupoint stimulation may engage peripheral afferents and autonomic reflex circuits (including vagal modulation) that influence central emetic networks and gastrointestinal motility [24, 25]. In addition, relevant alkaloids in processed Pinellia and sesquiterpene lactones such as dehydrocostus lactone from

Aucklandia may contribute to synergistic antiemetic actions by regulating gastrointestinal smooth muscle activity and neurotransmitter-related signaling [21, 26].

Clinically, the patch represents a non-invasive adjunct that can be integrated into routine prophylaxis without substantial complexity [27]. The NNT values (≈ 6 in ITT and ≈ 5 in PP) indicate a clinically meaningful incremental benefit for preventing moderate-to-severe CINV on top of dual antiemetic therapy, a regimen that remains widely used for MEC in real-world settings. Safety and tolerability were favorable: local skin reactions were uncommon and identical in both exposures (1.1%), no serious adverse events occurred, and rescue antiemetic use beyond the protocol regimen did not differ significantly between conditions. Because this external topical preparation does not require gastrointestinal absorption or hepatic/renal metabolism, it is particularly advantageous for patients who prefer to avoid additional oral medications, who have poor tolerance to systemic antiemetic drugs, or who have compromised hepatic or renal function. Such features support pragmatic implementation across diverse clinical workflows.

To reflect contemporary practice, some participants received chemotherapy plus a single targeted agent or immune checkpoint inhibitor: in the ITT set, 13/96 participants received combination targeted/immunotherapy (bevacizumab 7, trastuzumab 1, sintilimab 1, cetuximab 2, tislelizumab 2), and in the PP set, 12/68 did so (bevacizumab 6, trastuzumab 1, sintilimab 1, cetuximab 2, tislelizumab 2). Because of the crossover design, each participant's concomitant systemic therapy remained identical under both exposures, limiting confounding from imbalance. Updated emetogenic-risk frameworks generally classify many targeted agents and immune checkpoint inhibitors as having low or minimal emetogenic potential [28, 29], and their proportion in this trial was small; therefore, they are unlikely to explain the observed treatment effect.

Attrition remains a common challenge in multi-cycle crossover trials [13]. The overall dropout rate in this study was 29.2% (28/96). Most discontinuations occurred before the second period and were mainly due to refusal to continue, treatment plan changes, or clinical deterioration; only one participant discontinued due to a mild rash. Dropout was not significantly associated with Grade ≥ 2 CINV ($P = 0.35$). Despite missingness, the concordance of the ITT analyses (with MICE), PP analyses, and GLMM robustness analyses robustly supports our conclusions.

Several limitations should be considered. First, the study evaluated N-JZP on the background of dual antiemetic therapy in patients receiving MEC; its incremental benefit when added to contemporary triple or quadruple prophylaxis, or among patients receiving highly emetogenic chemotherapy, remains unknown. Second, the day 3 and day 7 assessments were selected to capture delayed symptom burden but did not allow detailed daily characterization of acute and delayed CINV trajectories. Third, participants were recruited from hospitals in North China, which may limit generalizability to other regions and healthcare systems. Finally, the trial focused on short-term efficacy and safety within two chemotherapy cycles; longer-term outcomes, including sustained quality-of-life benefit, chemotherapy adherence, and patient preference, require further study.

Future research should include large-scale, nationwide multicenter randomized controlled trials to confirm the efficacy of the patch across different emetogenic risk categories and diverse anticancer treatment modalities. Mechanistic studies incorporating more frequent follow-up time points, measurements of relevant biomarkers and neurotransmitters, and the identification of subgroups most likely to benefit are warranted. In addition, animal experiments and molecular investigations may further elucidate the synergistic antiemetic pathways underlying herbal constituents and acupoint stimulation, thereby providing a stronger scientific basis for the precision prevention and management of CINV using integrative Chinese medicine approaches.

Conclusion

In patients receiving moderately emetogenic chemotherapy, N-JZP applied to PC6, ST36, and CV8 as an adjunct to standard dual antiemetic therapy significantly reduced the risk of moderate-to-severe CINV compared with a sham patch. The intervention was safe, noninvasive, and easy to administer, with minimal local skin reactions and no increase in rescue antiemetic use. These findings support N-JZP as a feasible adjunctive symptom-control intervention in oncology supportive care.

Abbreviations

5-HT: 5-hydroxytryptamine
ARR: absolute risk reduction
CI: confidence interval
CONSORT: Consolidated Standards of Reporting Trials
CTCAE: Common Terminology Criteria for Adverse Events
ECOG: Eastern Cooperative Oncology Group
FLIE: Functional Living Index-Emesis
MICE: multiple imputation by chained equations
N-JZP: Novel Jiangni Zhitu Patch
NNT: number needed to treat
OR: odds ratio
TCM: Traditional Chinese Medicine
VAS: visual analog scale
WHO: World Health Organization

Declarations

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Competing interests

G.Y. is an inventor of the patented herbal formulation used in this study (Patent No. CN104189792B). Other inventors of the patent are not authors of this manuscript. No other authors declare any competing interests.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine (No. 2024BL02-026-02), Jiaozuo Second People's Hospital Medical Ethics Review Committee (No. KY2024-11-050), Medical Ethics Committee of the First Affiliated Hospital of Hebei North University (No. K2024315), Medical Ethics Committee of Shunyi Hospital of Beijing Hospital of Traditional Chinese Medicine (No. 2024SYKY19-01), and Medical Research Ethics Committee of Weifang Hospital of Traditional Chinese Medicine (No. 2024YX202). All participants provided written informed consent prior to enrollment.

Consent for publication

Not applicable.

Data availability

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

Materials availability

The patent herbal acupoint patches and sham patches are available from the corresponding author on reasonable request.

Code availability

The R scripts used for GEE analysis and MICE imputation are available from the corresponding author on reasonable request.

Author contribution

G.Y. and G.Z. conceptualized and designed the study. X.Z., S.L., Z.L., X.H., J.Z., L.L., L.L., and H.Z. performed clinical data collection and patient follow-up. J.H. and T.W. conducted the statistical analysis. X.Z. drafted the manuscript. S.C. critically revised and edited the final manuscript. All authors have read and approved the final manuscript.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Gemini and ChatGPT in order to improve the English language, enhance readability, and format the manuscript and code. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Figures

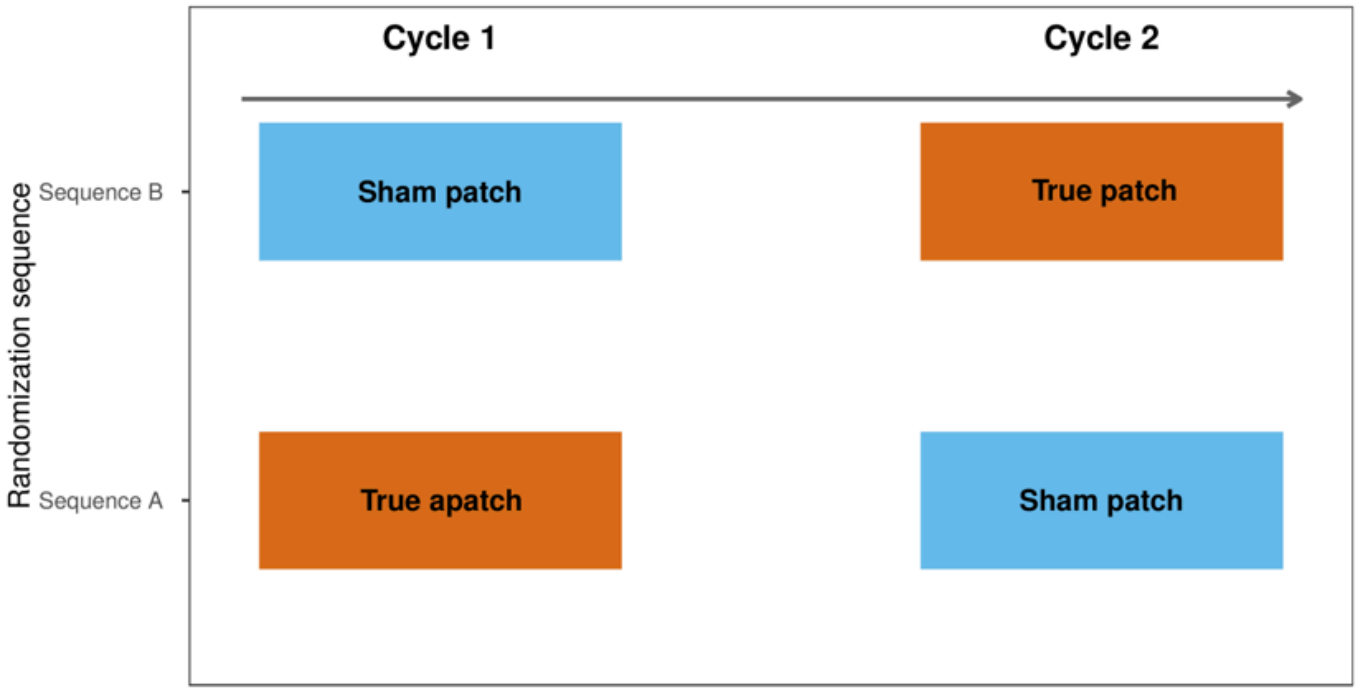


Figure 1

Schematic diagram of the study design.

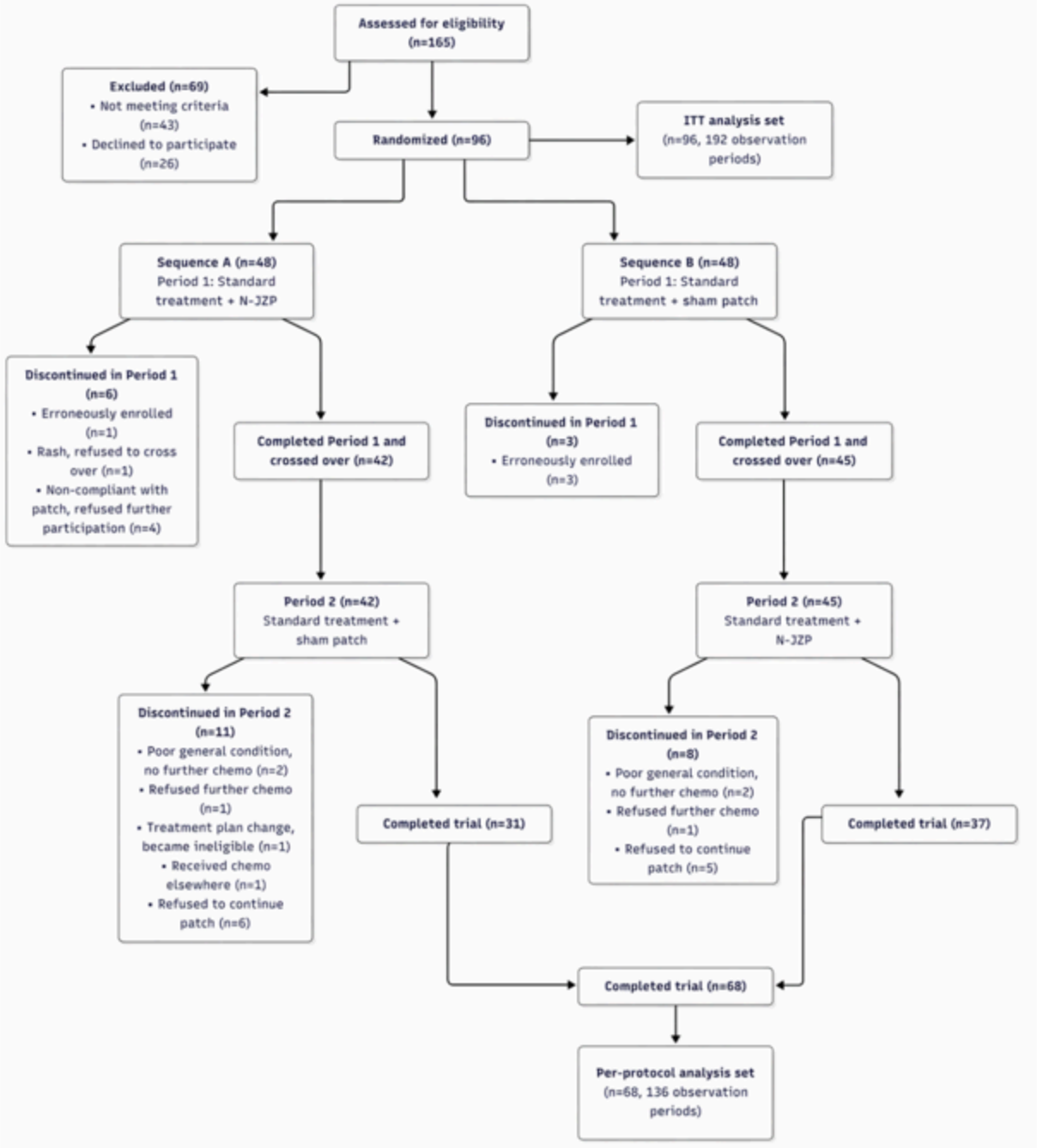


Figure 2

CONSORT crossover flow diagram.

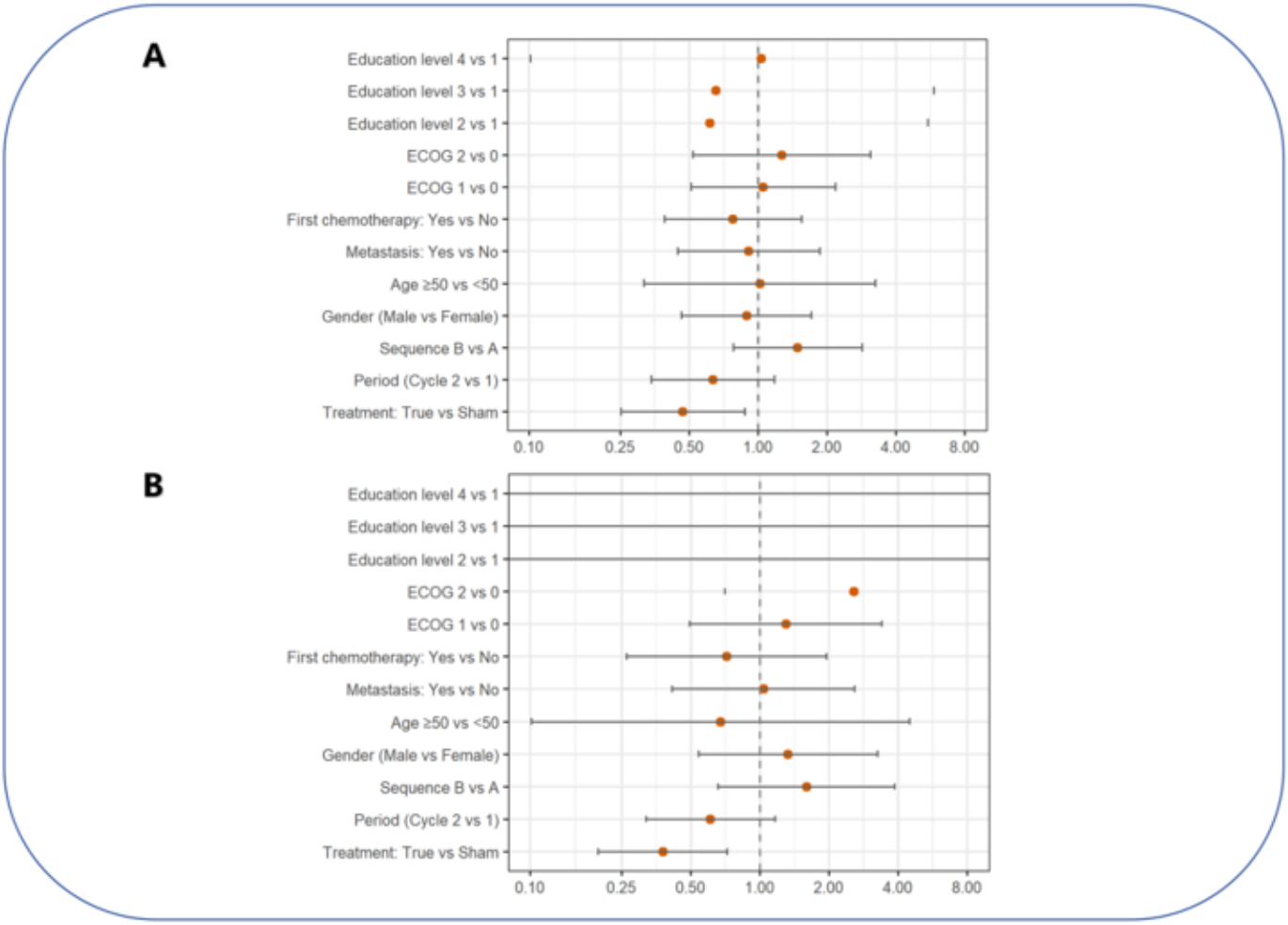


Figure 3

Forest plots illustrating the adjusted odds ratios for the incidence of Grade ≥ 2 CINV using the generalized estimating equations (GEE) model. **(A)**Intention-to-treat (ITT) population. **(B)** Per-protocol (PP) population.

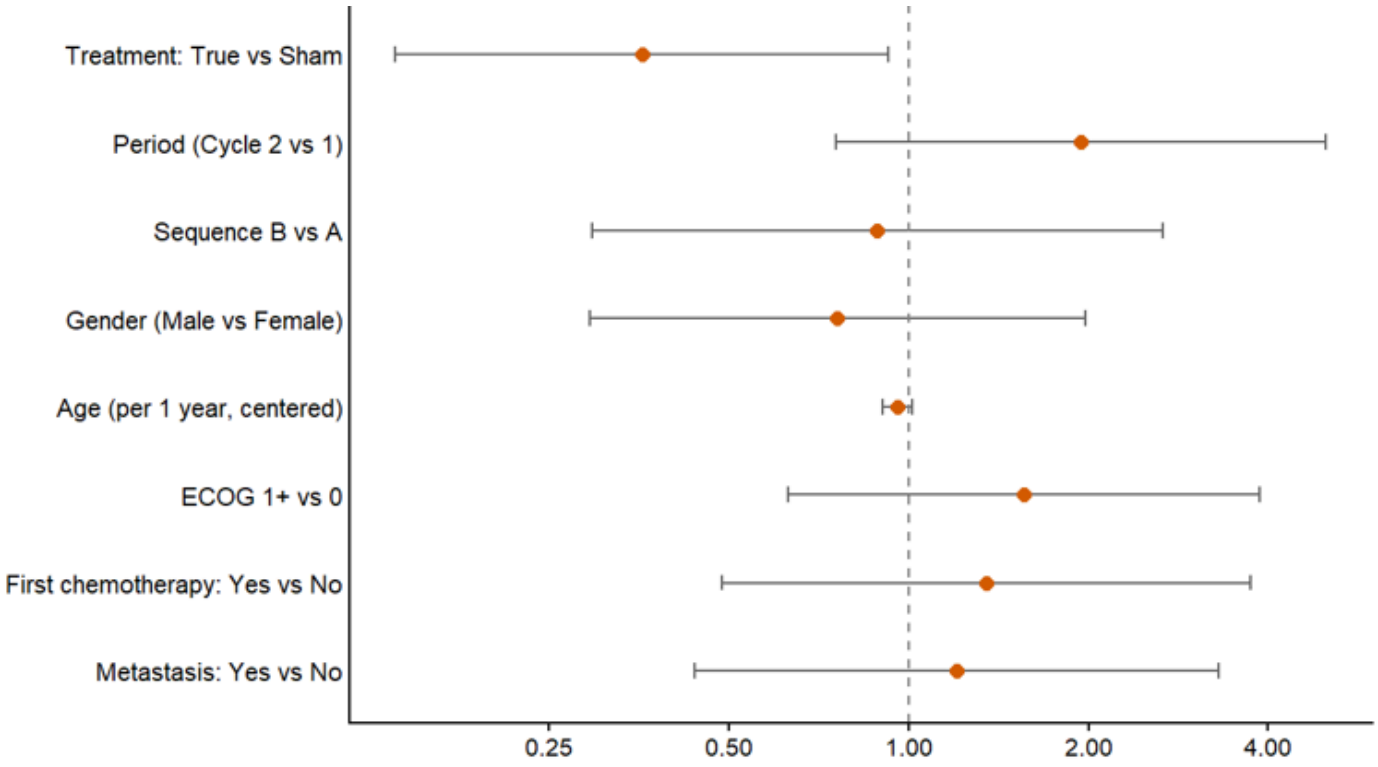


Figure 4

Forest plot illustrating the adjusted odds ratios for the incidence of any-grade (Grade ≥ 1) CINV in the PP population.