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Moxibustion at Neiguan acupoint in the prevention of myocardial damage caused by chemotherapy in breast cancer

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Abstract: Objective To investigate the effect of moxibustion on Neiguan acupoint in preventing myocardial damage caused by anthracycline-based chemotherapy in breast cancer patients, and to explore the feasibility of moxibustion on Neiguan acupoint in reducing cardiotoxicity induced by chemotherapy. **Methods** A total of 80 breast cancer patients who underwent adjuvant chemotherapy with EC-T (pirarubicin + cyclophosphamide followed by docetaxel) regimen after surgery in the Department of Breast Cancer, Shaanxi Provincial Cancer Hospital from May 2020 to May 2021 were selected and divided into control group (n=40) and experimental group (n=40) randomly. During the first four cycles of chemotherapy, both groups received dexrazoxane on the same day as pirarubicin. The experimental group received moxibustion on Neiguan acupoint for three consecutive days starting one day before chemotherapy. The electrocardiograms, cardiac function, levels of cardiac troponin I (cTnI), N-terminal pro-brain natriuretic peptide (NT-proBNP), and Karnofsky Performance Status (KPS) scores were observed before and after four cycles of chemotherapy. **Results** After four cycles of chemotherapy, the incidence of arrhythmia [22.5% (9/40) *vs* 50.0% (20/40), χ^2=6.545, P=0.011] and QRS wave voltage decrease [27.5% (11/40) *vs* 55.0% (22/40), χ^2=6.241, P=0.012] in the experimental group were lower than those in the control group. The cardiac function classification in the experimental group was better than that in the control group (Z=2.388, P=0.017). After four cycles of chemotherapy, left ventricular ejection fraction (LVEF) decreased and left ventricular end-diastolic diameter (LVEDD) increased in the control group, while LVEF and LVEDD changes in the experimental group were not significant. The cTnI levels, NT-proBNP levels, and KPS scores increased in both groups, and LVEF, LVEDD, cTnI levels, NT-proBNP levels, and KPS scores were better in the experimental group than those in the control group (P<0.05). **Conclusion** Moxibustion on Neiguan acupoint has a significant protective effect on myocardial damage caused by chemotherapy in breast cancer patients, and can further improve myocardial function on the basis of dexrazoxane.

Keywords: Moxibustion; Neiguan acupoint; Breast cancer; Chemotherapy; Pirarubicin; Dexrazoxane; Myocardial damage; Cardiac troponin; Brain natriuretic peptide; Cardiotoxicity
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Breast cancer ranks first in the incidence of female malignant tumors [1], and it is increasing year by year. At present, chemotherapy still plays an important role in improving the prognosis of breast cancer patients [2-3]. As the cornerstone of chemotherapy for breast cancer, anthracycline drugs, represented by epirubicin and pirarubicin, are widely used in clinical practice. However, a series of adverse reactions may occur during the use of anthracycline drugs, such as cardiac toxicity, bone marrow suppression, alopecia, peripheral neuropathy, etc., especially the cumulative dose cardiotoxicity [4-5], which may cause permanent damage to the heart, severely limiting their application [6-7]. In order to prevent myocardial damage caused by anthracycline drugs and reduce the adverse reactions of chemotherapy, dexamethasone was recommended to use during chemotherapy to reduce cardiac toxicity by chelating iron in anthracycline iron chelates. Although the effect is significant, most patients still cannot avoid myocardial injury [8]. Neiguan point is the collateral point of the Hand Jueyin Pericardium Meridian, and current research suggests that Neiguan is one of the most commonly used acupoints for treating myocardial injury [9-10]. In this paper, moxibustion at Neiguan point was used to prevent and reduce the cardiotoxicity caused by chemotherapy with anthracycline drugs in breast cancer patients.

1 Materials and Methods

1.1 General data

A total of 80 breast cancer patients who received postoperative adjuvant chemotherapy with EC-T (pirarubicin+cyclophosphamide docetaxel) scheme from May 2020 to May 2021 in the Breast Department of Shaanxi Cancer Hospital were selected, and they were divide into control group (n=40) and experimental group (n=40) according to the random number table. There was no significant difference between the two groups in age,

breast cancer stage, pathological type and other general information (P>0.05). **See Table 1.**

Tab.1 General data of two groups (n=40, case)

Item	Control group	Experiment group	$t/Z/\chi^2$ value	P value
Age	58.93±7.81	58.24±7.67	0.399	0.691
Tumor Stage				
I	13	12		
II	17	16	0.431	0.666
III	10	12		
Pathological Type				
Infiltrating lobular carcinoma	6	5		
Infiltrating ductal carcinoma	30	32	0.298	0.861
others	4	3		

Inclusion criteria: (1) invasive breast cancer confirmed by histopathology through fine-needle aspiration or surgery, and adjuvant chemotherapy of EC-T was conducted; (2) treatment was completed on time according to chemotherapy cycle plan; (3) Patient was able to tolerate chemotherapy and had no contraindications to chemotherapy in the pre-treatment evaluation; (4) The patient had good compliance and could receive follow-up on time; (5) Patients were willing to participate and cooperate; (6) All plans had been approved by the Ethics Committee of Shaanxi Cancer Hospital and have obtained informed consent from patients. This study was approved by the Ethics Committee of Shaanxi Cancer Hospital.

1.2 Methods

All patients were given an EC-T chemotherapy regimen, administered intravenously for one day in hospital, with one chemotherapy cycle every three weeks. Specific medication: pirarubicin 50 mg/m^2, cyclophosphamide 600 mg/m^2, and docetaxel 75 mg/m^2. During the first four cycles of chemotherapy, dexrazoxane (Jiangsu Aosaikang Pharm, H20061157, 250 mg) 900 mg/m^2 was used simultaneously on the same day that pirarubicin was used. The experimental group patients started moxibustion on Neiguan acupoint the day before chemotherapy, twice a day for three consecutive days.

1.3 Materials and drugs

(1) Aitiao: Shaanxi Yaowang Hometown Aiye Co., Ltd; (2) Cardiac troponin I(cTnI) and N-terminal pro-brain natriuretic peptide (NT-proBNP) ELISA kits: Beijing ZSGB-Bio.

1.4 Therapeutic effects

1.4.1 Acute phase

During the acute phase, the primary manifestation of acute cardiac toxicity is the changes in electrocardiogram and cardiac function in patients before and after chemotherapy. The classification criteria for cardiac function are as follows: Grade 0, normal; Grade I, asymptomatic but with abnormal cardiac signs; Grade II, transient cardiac insufficiency, no treatment required; Grade III, symptoms of heart failure, with effective treatment; Grade IV, symptoms of heart failure, with ineffective treatment [11]. In this study, grade 0 to I was classified as normal heart function and grade II to IV was classified as abnormal heart function. All patients underwent electrocardiogram examinations before and after 4 cycles of chemotherapy.

1.4.2 Chronic phase

During the chronic phase, the chronic cardiac toxicity was evaluated by the indicators as follows: (1) left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDD) through echocardiography. (2) cTnI and NT-proBNP detected by ELISA at one day before the first chemotherapy and one day before the fifth cycle of chemotherapy. (3) changes in Karnofsky Performance Status (KPS) scores between the patient's first admission and before the 5th cycle of chemotherapy.

1.5 Statistical analysis

Statistical analysis was conducted using SPSS 17.0 software. Counting data was represented by case (%), using chi-square test. Measurement data was expressed in $\overline{x} \pm s$, ANOVA test was used for inter group comparison, and LSD-t test was used for pairwise comparison. P<0.05 indicated a statistically significant difference.

2 Results

2.1 Comparison of ECG and cardiac function grading between two groups before and after 4 cycles of chemotherapy

There were 3 cases of ST-T abnormalities in the control group and 2 cases in the experimental group before chemotherapy, and no arrhythmia or QRS complex voltage drop occurred in both groups. The incidence of ST-T abnormalities after 4 cycles of chemotherapy was slightly lower in the experimental group than in the control group [22.5% (9/40) *vs* 42.5% (17/40), χ^2=3.647, *P*=0.056]. The incidence of arrhythmia [22.5% (9/40) *vs* 50.0% (20/40), χ^2=6.545, *P*=0.010] and QRS complex voltage drop [27.5% (11/40) *vs* 55.0% (22/40), χ^2=6.241, *P*=0.012] in the experimental group were lower than those in the control group. There was no statistically significant difference in cardiac function changes between the two groups before chemotherapy (*P*>0.05). After 4 cycles of chemotherapy, the heart function grading of the experimental group was better than that of the control group (*P*<0.05). **See Table 2.**

2.2 Comparison of cardiac function indicators between two groups before and after 4-cycle chemotherapy

There was no statistically significant difference in cardiac function indicators between the two groups before chemotherapy (*P*>0.05). After 4 cycles of chemotherapy, the control group's LVEF decreased and LVEDD increased, while the experimental group's LVEF and LVEDD did not show significant changes. The levels of cTnI, NT-proBNP, and Karnofsky functional status score (KPS) in both groups increased, and the LVEF, LVEDD, cTnI levels, NT-proBNP, and KPS in the experimental group were better than those in the control group (*P*<0.05). **See Table 3.**

Tab.2 Comparison of cardiac function score between two groups before and after chemotherapy (*n*=40, case)

Group	Pre-treatment					Post-treatment				
	0	I	II	III	IV	0	I	II	III	IV
Control Group	27	8	5	0	0	14	13	11	2	0
Experiment Group	24	12	4	0	0	23	12	5	0	0
***Z* value**	0.520					2.388				
***P* value**	0.603					0.017				

Tab.3 Comparison of cardiac function indicators between two groups before and after 4-cycle chemotherapy (*n*=40, case)

Group	Time	LVEF (%)	LVEDD (mm)	cTnI (ng/mL)	NT-proBNP (pg/mL)	KPS
Control Group	**Pre-Treatment**	77.24±4.45	43.36±3.71	0.07±0.02	65.32±16.89	59.13±5.98
	Post-Treatment	56.35±7.36[a]	49.34±1.54[a]	0.41±0.04[a]	351.11±48.38[a]	69.85±3.98
Experiment Group	**Pre-Treatment**	69.28±5.66	41.98±2.22	0.08±0.02	64.29±17.87	64.52±5.33
	Post-Treatment	67.88±5.98[b]	44.22±3.89[b]	0.16±0.05[ab]	129.77±31.97[ab]	85.22±3.95[ab]

3 Discussion

In 2015, a European study followed up 2 625 patients with breast cancer, and patients all received adjuvant chemotherapy containing anthracycline drugs. The results showed that about 9% of the patients had different degrees of cardiac toxicity, and about 98% of the patients had cardiac toxicity within the first year after chemotherapy [12]. If breast cancer patients receive anthracycline chemotherapy, it is particularly important to prevent cardiac toxicity in advance during the treatment process [13]. Dexrazoxane is the most effective drug in clinical practice for preventing cardiotoxicity caused by anthracycline chemotherapy drugs. Research has shown that as the only drug approved by the US FDA for the prevention and protection of cardiotoxicity caused by anthracycline chemotherapy drugs [14-15], the early use of dexamethasone can effectively reduce the risk of cardio toxicity in patients, and delay the onset of cardiotoxicity and increase the range of cumulative dose thresholds. However, dexamethasone cannot completely avoid the myocardial toxicity caused by anthracycline chemotherapy drugs [16]. With the increase of chemotherapy frequency and drug concentration, myocardial toxicity will still appear to varying degrees, which requires us to find more suitable preventive measures.

Chinese medicine has unique experience in

protecting against myocardial injury [17]. Moxibustion therapy, as a safe and effective treatment method, has been valued in the treatment of myocardial injury. A large amount of data confirms that moxibustion at Neiguan point has a protective effect on the heart, such as improving energy metabolism, promoting oxygen free radical clearance, activating endogenous protective substances, inhibiting neutrophils, calcium channel blockade, and inhibiting apoptosis, which can significantly reduce the degree of myocardial ischemia-reperfusion injury [18]. “Nei”, means internally, and "Guan" is a crucial level for the inner world. Stimulation of Neiguan point has the functions of calming the heart and calming the mind, harmonizing the stomach, regulating qi, relieving nausea and vomiting, relieving pain slowly, promoting obstruction and relieving depression, regulating yin and yang qi and blood, and unblocking meridians [19]. Lin *et al* [18] treated coronary heart disease patients with the Neiguan acupoint of the pointer, which relieved angina symptoms, improved electrocardiogram, and had a significant therapeutic effect. In this study, based on the use of dexrazoxane, breast cancer patients received adjuvant chemotherapy with EC-T scheme and moxibustion at Neiguan point, and found that the ECG changes and cardiac function of these patients were significantly improved, and the changes in serum cTnI and NT-proBNP of these patients were also better than those of patients who only used dexrazoxane, suggesting that moxibustion at Neiguan point can improve the performance of dexrazoxane, Further protect myocardial cells, thereby improving myocardial function.

In a word, moxibustion at Neiguan point can significantly reduce the incidence of myocardial damage in patients with breast cancer after chemotherapy, further improve myocardial function, and is easy to operate, with small side effects, and is economical and practical.

Conflict of interest: None

References

[1] Waks AG, Winer EP. Breast cancer treatment: a review[J]. JAMA, 2019, 321(3): 288-300.

[2] Di Nardo P, Lisanti C, Garutti M, et al. Chemotherapy in patients with early breast cancer: clinical overview and management of long-term side effects[J]. Expert Opin Drug Saf, 2022, 21(11): 1341-1355.

[3] Zhou SY, Zhu AP, Zhang H, et al. Curative effect of EC-wP neoadjuvant chemotherapy on HER2 negative breast cancer and the risk factors of recurrence and metastasis[J]. Chin J Clin Res, 2022, 35(9): 1216-1220. **[In Chinese]**

[4] Conte B, Montemurro F, Levaggi A, et al. Anthracycline, taxane, and trastuzumab-based neoadjuvant chemotherapy in HER2-positive early breast cancer: phase II trial[J]. Tumori, 2023, 109(1): 71-78.

[5] Cao SH, Xue JX, Chen L, et al. Effects of the Chinese herbal medicine Hong Huang Decoction, on myocardial injury in breast cancer patients who underwent anthracycline-based chemotherapy[J]. Front Cardiovasc Med, 2022, 9: 921753.

[6] Liu C, Cheng BL, Zhao G, et al. Process analysis of anthracycline adverse reactions in breast cancer patients with postoperative chemotherapy[J]. J Investig Med, 2022, 70(6): 1352-1357.

[7] Kwon SS, Nam BD, Lee MY, et al. Increased EAT volume after anthracycline chemotherapy is associated with a low risk of cardiotoxicity in breast cancer[J]. Breast Cancer Res Treat, 2022, 196(1): 111-119.

[8] de Baat EC, Mulder RL, Armenian S, et al. Dexrazoxane for preventing or reducing cardiotoxicity in adults and children with cancer receiving anthracyclines[J]. Cochrane Database Syst Rev, 2022, 9(9): CD014638.

[9] Xue Y, Wu S, Li J, et al. Research progress of acupuncture on PC6 on regulation of central mechanisms on myocardial ischemia[J]. Chin J Basic Med Tradit Chin Med, 2017, 23(4): 592-594. **[In Chinese]**

[10] Yan CA, Cheng GY, Zhang Q, et al. Discussion on the mechanism and clinical application progress of Neiguan acupoint therapy for coronary heart disease based on “treatment of cardiothoracic diseases by using PC6”[J]. Pract J Card Cereb Pneumal Vasc Dis, 2023, 31(4): 107-110. **[In Chinese]**

[11]Xu L. Experimental study about prevention of anthracycline-induced myocardial injury by ginger moxibustion[J]. China Mod Dr, 2016, 54(28): 139-141. **[In Chinese]**

[12] Gu J, Wang D, Jiang L, et al. Assessment of global cardiac function using AutoSTRAIN automatic strain quantitative technology in patients with breast cancer undergoing anthracycline-based chemotherapy[J]. Ultrasound Med Biol, 2023, 49(1): 368-374.

[13] Shima H, Kutomi G, Kuga Y, et al. Additional effect of anthracycline in preoperative chemotherapy with a sequential anthracycline-containing regimen preceded by pertuzumab, trastuzumab and docetaxel combination therapy[J]. Exp Ther Med, 2022, 25(1): 68.

[14] Alam MS, Sultana A, Wang GH, et al. Gene expression profile analysis to discover molecular signatures for early diagnosis and therapies of triple-negative breast cancer[J]. Front Mol Biosci, 2022, 9: 1049741.

[15] Tan RP, Cong T, Xu GW, et al. Anthracycline-induced atrial structural and electrical remodeling characterizes early cardiotoxicity and contributes to atrial conductive instability and dysfunction[J]. Antioxid Redox Signal, 2022, 37(1/2/3): 19-39.

[16] Leong DP, Lenihan DJ. Clinical practice guidelines in cardio-oncology[J]. Heart Fail Clin, 2022, 18(3): 489-501.

[17] Gao H, Wu PX, Xiao LY, et al. Efficacy and safety of acupoint stimulation in the treatment of angina pectoris caused by coronary heart disease: a meta-analysis[J]. Chin J Gen Pract, 2023, 21(4): 698-703. **[In Chinese]**

[18] Mu XY, Song YH, Zhang D, et al. Preconditioning of needling PC6 improving MIRI: a study of research progress[J]. J Clin Acupunct Moxibustion, 2018, 34(10): 75-79. **[In Chinese]**

[19] Li XL, Nie SP, Li A, et al. Research progress on the mechanism of acupuncture at nèiguān in the treatment of mental disorders based on functional magnetic resonance imaging[J]. China Med Her, 2021, 18(20): 34-37. **[In Chinese]**

[20] Lin LZ, Liang ZZ, Chen JX. Clinical observation on acupoint pointer in stable angina pectoris of coronary heart disease[J]. China Med Her, 2010, 7(22): 126-128. **[In Chinese]**

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·论　著·

艾灸内关穴对乳腺癌化疗所致心肌损害的预防作用

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摘要：目的　研究艾灸内关穴在预防乳腺癌含蒽环类药物化疗所致心肌损害中的作用，探索艾灸内关穴减轻化疗心脏毒性的可行性。**方法**　选取陕西省肿瘤医院乳腺科 2020 年 5 月至 2021 年 5 月收治的行 EC-T（吡柔比星+环磷酰胺序贯多西他赛）方案术后辅助化疗的乳腺癌患者 80 例，依据随机数表法分为对照组 40 例和试验组 40 例。两组患者在前 4 周期化疗过程中，使用吡柔比星药物当天均同时使用右雷佐生；试验组患者于化疗前 1 天开始进行艾灸内关穴，每天 2 次，连续 3 d。观察两组患者 4 周期化疗前后的心电图、心功能、血肌钙蛋白 I（cTnI）和N 末端脑钠肽前体（NT-proBNP）水平，以及 Karnofsky 功能状态评分（KPS）的变化。**结果**　4 周期化疗后，心律异常发生率[22.5%（9/40）*vs* 50.0%（20/40），$\chi^2=6.545$，$P=0.010$]和 QRS 波群电压下降发生率试验组均低于对照组[27.5%（11/40）*vs* 55.0%（22/40），$\chi^2=6.241$，$P=0.012$]。化疗后试验组心功能分级优于对照组（$Z=2.388$，$P=0.017$）。4 周期化疗后，对照组左心室射血分数（LVEF）下降、左室舒张末期内径（LVEDD）增大，试验组 LVEF、LVEDD 变化不明显，两组 cTnI 和 NT-proBNP 水平及 KPS 评分均升高，且试验组 LVEF、LVEDD、cTnI 和 NT-proBNP 水平及 KPS 评分均优于对照组（$P<0.05$）。**结论**　艾灸内关穴对于乳腺癌含蒽环类药物化疗所致心肌损害具有明显的保护作用，可以在右雷佐生作用的基础上进一步改善心肌功能。

关键词： 艾灸；内关穴；乳腺癌；化疗；吡柔比星；右雷佐生；心肌损害；肌钙蛋白；脑钠肽；心脏毒性

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Abstract: Objective　To investigate the effect of moxibustion on Neiguan acupoint in preventing myocardial damage caused by anthracycline-based chemotherapy in breast cancer patients, and to explore the feasibility of moxibustion on Neiguan acupoint in reducing cardiotoxicity induced by chemotherapy. **Methods**　A total of 80 breast cancer patients who underwent adjuvant chemotherapy with EC-T (pirarubicin + cyclophosphamide followed by docetaxel) regimen after surgery in the Department of Breast Cancer, Shaanxi Provincial Cancer Hospital from May 2020 to May 2021 were selected and divided into control group ($n=40$) and experimental group ($n=40$) randomly. During the first four cycles of chemotherapy, both groups received dexrazoxane on the same day as pirarubicin. The experimental group received moxibustion on Neiguan acupoint for three consecutive days starting one day before chemotherapy. The electrocardiograms, cardiac function, levels of cardiac troponin I (cTnI), N-terminal pro-brain natriuretic peptide (NT-proBNP), and Karnofsky Performance Status (KPS) score were observed before and after four cycles of chemotherapy. **Results**　After four cycles of chemotherapy, the incidences of arrhythmia [22.5%(9/40) *vs* 50.0%(20/40), $\chi^2=6.545$, $P=0.011$] and QRS wave voltage decrease[27.5%(11/40) *vs* 55.0%(22/40), $\chi^2=6.241$, $P=0.012$] in the experimental group were lower than those in the control group. The cardiac function classification in the

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experimental group was better than that in the control group (Z=2.388,P<0.017). After four cycles of chemotherapy, left ventricular ejection fraction (LVEF) decreased and left ventricular end-diastolic diameter (LVEDD) increased in the control group, while LVEF and LVEDD changes were not significant in the experimental group. The cTnI levels, NT-proBNP levels, and KPS scores increased in both groups, and LVEF, LVEDD, cTnI, NT-proBNP levels, and KPS scores were better in the experimental group than those in the control group (P<0.05). **Conclusion** Moxibustion on Neiguan acupoint has a significant protective effect on myocardial damage caused by chemotherapy in breast cancer patients, and can further improve myocardial function on the basis of dexrazoxane.

Keywords: Moxibustion; Neiguan acupoint; Breast cancer; Chemotherapy; Pirarubicin; Dexrazoxane; Myocardial damage; Cardiac troponin; Brain natriuretic peptide; Cardiotoxicity

Fund program: Key Research and Development Project of Shaanxi Province (2021SF-218)

乳腺癌在女性恶性肿瘤发病率中位居第一位[1],并且呈逐年上升趋势。目前乳腺癌的治疗中,化疗对于改善乳腺癌患者预后依然有着举足轻重的作用[2-3]。作为乳腺癌化疗的基础药物,以表柔比星、吡柔比星等为代表的蒽环类药物在临床中应用广泛,但该类药物在使用过程中可能产生的一系列不良反应,诸如心脏毒性、骨髓抑制、脱发和周围神经病变等,特别是剂量累积性心脏毒性[4-5],可能会造成心脏的永久性损伤,严重限制了该类药物的使用剂量[6-7]。为了预防蒽环类药物引起的心肌损害,降低化疗带来的副作用,指南推荐在化疗的过程中使用右雷佐生,其通过络合蒽环-铁螯合物中的铁以减轻心脏毒性,虽然效果显著,但大部分患者最终仍有心肌损害的发生[8]。内关穴是手厥阴心包经的络穴,目前的研究认为内关是治疗心肌损伤常用的穴位之一[9-10]。本研究对乳腺癌化疗患者艾灸内关穴,探索预防及降低使用蒽环类药物化疗所引起的心脏毒性的方法。现报道如下。

1　资料与方法

1.1　一般资料　选取陕西省肿瘤医院乳腺科 2020 年 5 月至 2021 年 5 月收治的行 EC-T(吡柔比星+环磷酰胺序贯多西他赛)方案术后辅助化疗的乳腺癌患者 80 例,依据随机数表法分为对照组 40 例和试验组 40 例。两组年龄、乳腺癌分期及病理类型等一般资料比较,差异无统计学意义(P>0.05)。见表 1。

纳入标准:(1) 均经穿刺或者手术等方式获得组织病理学证实的浸润性乳腺癌,且符合指南要求需要进行 EC-T 方案辅助化疗;(2) 能按照既定的化疗周期计划按时完成治疗;(3) 通过治疗前评估,患者身体能耐受化疗,无化疗禁忌证;(4) 患者依从性良好,能按时接受随访;(5)患者愿意参与,并配合;(6) 获得患者的知情同意。排除标准:不符合上述任何一条标准均排除。本研究经陕西省肿瘤医院伦理委员会批准。

表 1　两组患者一般资料　(n=40, 例)
Tab. 1　General data of two groups　(n=40, case)

项目	对照组	试验组	$t/Z/\chi^2$ 值	P 值
年龄(岁, $\bar{x}\pm s$)	58.93±7.81	58.24±7.67	0.399	0.691
乳腺癌分期				
Ⅰ	13	12		
Ⅱ	17	16	0.431[a]	0.666
Ⅲ	10	12		
病理类型				
浸润性小叶癌	6	5		
浸润性导管癌	30	32	0.298[b]	0.861
其他	4	3		

注:[a] 为秩和检验;[b] 为 χ^2 检验。

1.2　方法　两组患者均给予 EC-T 化疗方案,静脉滴入,住院 1 天用药,每 3 周为 1 个化疗周期,具体:吡柔比星 50 mg/m^2,环磷酰胺 600 mg/m^2,多西他赛 75 mg/m^2。两组患者在前 4 周期化疗过程中,使用吡柔比星当天均同时使用右雷佐生(江苏奥赛康药业,国药准字 H20061157,250 mg/支)900 mg/m^2;试验组患者于化疗前 1 天开始进行艾灸内关穴,每天 2 次,连续 3 d。

1.3　材料与药物　(1) 艾条:陕西药王故里艾业;(2) 心肌肌钙蛋白 I(cardiac troponin Ⅰ, cTnI)和 N 末端脑钠肽(N-terminal pro-brain natriuretic peptide, NT-proBNP)酶联免疫吸附试验(enzyme-linked immunosorbent assay, ELISA)试剂盒:北京中杉金桥生物技术。

1.4　疗效观察

1.4.1　急性期　急性心脏毒性首要表现在化疗前后患者心电图和心功能分级的改变。心功能分级标准如下:0 级,正常;Ⅰ级,无症状但又有异常心脏征象;Ⅱ级,虽有短暂的心功能不足,但不需治疗;Ⅲ级,有症状和心功能不足表现,治疗有效;Ⅳ级,有症状,心功能不足,治疗无效[11]。本研究将 0~Ⅰ级计为正常心功能,Ⅱ~Ⅳ级计为异常心功能。两组患者 4 周期

化疗前后分别行心电图检查。

1.4.2　慢性期　慢性心脏毒性主要依据心功能相关指标:(1) 通过心脏彩超检测左心室射血分数(left ventricular ejection fraction, LVEF)和左室舒张末期内径(left ventricular end diastolic dimension, LVEDD)改变;(2) 采用 ELISA 法检测首次化疗前 1 天、第 5 周期化疗前 1 天的 cTnI 和 NT-proBNP 水平;(3) 对比患者首次入院和第 5 周期化疗前的 Karnofsky 功能状态(Karnofsky Performance Status, KPS)评分变化。

1.5　统计学方法　采用 SPSS 17.0 软件进行统计学分析。计数资料采用例(%)表示,比较采用 χ^2 检验;计量资料以 $\bar{x}\pm s$ 表示,比较采用成组 t 检验和配对 t 检验;等级资料的比较采用秩和检验。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　4 周期化疗前后两组患者的心电图及心功能分级比较　化疗前 ST-T 异常对照组 3 例,试验组 2 例,两组无心律异常、QRS 波群电压下降发生。4 周期化疗后 ST-T 异常发生率试验组略低于对照组,差异无统计学意义[22.5%(9/40) *vs* 42.5%(17/40), $\chi^2=3.647$, $P=0.056$];心律异常发生率[22.5%(9/40) *vs* 50.0%(20/40), $\chi^2=6.545$, $P=0.010$]、QRS 波群电压下降发生率试验组低于对照组[27.5%(11/40) *vs* 55.0%(22/40), $\chi^2=6.241$, $P=0.012$]。化疗前两组患者的心功能分级比较差异无统计学意义($P>0.05$)。4 周期化疗后试验组心功能分级优于对照组($P<0.05$)。见表 2。

2.2　两组患者 4 周期化疗前后心功能指标比较　化疗前两组心功能指标差异无统计学意义($P>0.05$)。4 周期化疗后,对照组 LVEF 下降、LVEDD 增大,试验组 LVEF 、LVEDD 变化不明显;两组 cTnI 和 NT-proBNP 水平及 KPS 评分均升高,且试验组 LVEF、LVEDD、cTnI 和 NT-proBNP 水平及 KPS 评分均优于对照组($P<0.05$)。见表 3。

表 2　两组化疗前后心功能分级比较　($n=40$, 例)

Tab. 2　Comparison of cardiac function score between two groups before and after chemotherapy　($n=40$, case)

组别	治疗前					治疗后				
	0	Ⅰ	Ⅱ	Ⅲ	Ⅳ	0	Ⅰ	Ⅱ	Ⅲ	Ⅳ
对照组	27	8	5	0	0	14	13	11	2	0
试验组	24	12	4	0	0	23	12	5	0	0
Z 值			0.520					2.388		
P 值			0.603					0.017		

表 3　两组 4 周期化疗前后心功能指标比较　($n=40$, $\bar{x}\pm s$)

Tab. 3　Comparison of cardiac function indicators between two groups before and after 4-cycle chemotherapy　($n=40$, $\bar{x}\pm s$)

组别	时间	LVEF(%)	LVEDD (mm)	cTnI (ng/mL)	NT-proBNP (pg/mL)	KPS 评分
对照组	化疗前	77.24±4.45	43.36±3.71	0.07±0.02	65.32±16.89	59.13±5.98
	化疗后	56.35±7.36[a]	49.34±1.54[a]	0.41±0.04[a]	351.11±48.38[a]	69.85±3.98
试验组	化疗前	69.28±5.66	41.98±2.22	0.08±0.02	64.29±17.87	64.52±5.33
	化疗后	67.88±5.98[b]	44.22±3.89[b]	0.16±0.05[ab]	129.77±31.97[ab]	85.22±3.95[ab]

注:与化疗前比较,[a]$P<0.05$;与对照组比较,[b]$P<0.05$。

3　讨　论

2015 年欧洲的一项研究对 2 625 例乳腺癌患者进行了随访,纳入的患者均进行了含蒽环类药物的辅助化疗,结果提示约 9%的患者发生了不同程度的心脏毒性,其中约 98%的患者在化疗后的第 1 年内即出现了心脏毒性[12]。由此可见,乳腺癌患者若接受蒽环类化疗,在治疗过程中,对心脏毒性的关注和提前预防显得尤为重要[13]。右雷佐生是临床中用于预防蒽环类化疗药物所导致的心脏毒性最有效的药物。研究表明,作为美国食品药品监督管理局批准的唯一用于预防蒽环类化疗药物所致心脏毒性的药物[14-15],右雷佐生的尽早使用,可有效降低该类患者心脏毒性风险,并可使其出现心脏毒性时间延后,剂量累计阈值范围增大。尽管如此,右雷佐生却不能完全避免蒽环类化疗药物所导致的心肌毒性[16],随着化疗次数的增加,药物浓度的蓄积,心肌毒性仍会不同程度的出现,这就需要寻找更合适的预防手段。

中医对于心肌损伤保护方面有着独特的经验[17],艾灸疗法作为一种安全有效的治疗手段在心肌损伤治疗中越来越受到人们重视。大量的数据证实,艾灸内关穴对心脏具有保护作用,如改善能量代谢、促进氧自由基清除、激活内源型保护物质、抑制中性粒细胞、钙通道阻滞和抑制凋亡等,能明显降低心肌缺血再灌注损伤的程度[18]。“内”,内部也;“关”,关卡也,此穴为内在之关要也。刺激内关穴有宁心安神、和胃降逆、宽胸理气、降逆止呕、缓急止痛、宣痹解郁、调补阴阳气血、疏通经脉等作用[19]。林连枝[20]采用指针内关穴治疗冠状动脉粥样硬化性心脏病(冠心病)患者,心绞痛症状缓解,心电图改善,疗效显著。本研究中,在使用右雷佐生的基础上,对接受 EC-T 方案进行辅助化疗的乳腺癌患者联合艾灸内关穴治疗后,发现患者的心电图变化和心功能情况均有明显改善,且患者的血清 NT-proBNP 变化也优于单纯使用右雷佐生的患者,提示艾灸内关穴能在右雷佐生的基础上,进一步保护心肌细胞,从而改善心肌

功能。

总之,艾灸内关穴,可明显降低乳腺癌患者化疗后心肌损害的发生率,可进一步改善心肌功能。

利益冲突　无

参考文献

[1] Waks AG, Winer EP. Breast cancer treatment: a review[J]. JAMA, 2019, 321(3): 288-300.

[2] Di Nardo P, Lisanti C, Garutti M, et al. Chemotherapy in patients with early breast cancer: clinical overview and management of long-term side effects[J]. Expert Opin Drug Saf, 2022, 21(11): 1341-1355.

[3] 周帅跃,朱爱萍,张煌,等.EC-wP 新辅助化疗 HER2 阴性乳腺癌的疗效及复发转移的危险因素[J].中国临床研究,2022,35(9):1216-1220.
Zhou SY, Zhu AP, Zhang H, et al. Curative effect of EC-wP neoadjuvant chemotherapy on HER2 negative breast cancer and the risk factors of recurrence and metastasis[J]. Chin J Clin Res, 2022, 35(9): 1216-1220.

[4] Conte B, Montemurro F, Levaggi A, et al. Anthracycline, taxane, and trastuzumab-based neoadjuvant chemotherapy in HER2-positive early breast cancer: phase Ⅱ trial[J]. Tumori, 2023, 109(1): 71-78.

[5] Cao SH, Xue JX, Chen L, et al. Effects of the Chinese herbal medicine Hong Huang Decoction, on myocardial injury in breast cancer patients who underwent anthracycline-based chemotherapy[J]. Front Cardiovasc Med, 2022, 9: 921753.

[6] Liu C, Cheng BL, Zhao G, et al. Process analysis of anthracycline adverse reactions in breast cancer patients with postoperative chemotherapy[J]. J Investig Med, 2022, 70(6): 1352-1357.

[7] Kwon SS, Nam BD, Lee MY, et al. Increased EAT volume after anthracycline chemotherapy is associated with a low risk of cardiotoxicity in breast cancer[J]. Breast Cancer Res Treat, 2022, 196(1): 111-119.

[8] de Baat EC, Mulder RL, Armenian S, et al. Dexrazoxane for preventing or reducing cardiotoxicity in adults and children with cancer receiving anthracyclines[J]. Cochrane Database Syst Rev, 2022, 9(9): CD014638.

[9] 薛艳,吴松,李佳,等.针刺内关穴对心肌缺血中枢神经调节作用的研究进展[J].中国中医基础医学杂志,2017,23(4):592-594.
Xue Y, Wu S, Li J, et al. Research progress of acupuncture on PC6 on regulation of central mechanisms on myocardial ischemia[J]. Chin J Basic Med Tradit Chin Med, 2017, 23(4): 592-594.

[10] 闫慈爱,程光宇,张奇,等.基于“心胸内关谋”探讨内关穴位疗法治疗冠心病的机制及临床应用进展[J].实用心脑肺血管病杂志,2023,31(4):107-110.
Yan CA, Cheng GY, Zhang Q, et al. Discussion on the mechanism and clinical application progress of Neiguan acupoint therapy for coronary heart disease based on \\“treatment of cardiothoracic diseases by using PC6\\”[J]. Pract J Card Cereb Pneumal Vasc Dis, 2023, 31(4): 107-110.

[11] 徐璐.隔姜艾灸预防蒽环类药物所致心肌损害的实验研究[J].中国现代医生,2016,54(28):139-141.
Xu L. Experimental study about prevention of anthracycline-induced myocardial injury by ginger moxibustion[J]. China Mod Dr, 2016, 54(28): 139-141.

[12] Gu J, Wang D, Jiang L, et al. Assessment of global cardiac function using AutoSTRAIN automatic strain quantitative technology in patients with breast cancer undergoing anthracycline-based chemotherapy[J]. Ultrasound Med Biol, 2023, 49(1): 368-374.

[13] Shima H, Kutomi G, Kuga Y, et al. Additional effect of anthracycline in preoperative chemotherapy with a sequential anthracycline-containing regimen preceded by pertuzumab, trastuzumab and docetaxel combination therapy[J]. Exp Ther Med, 2022, 25(1): 68.

[14] Alam MS, Sultana A, Wang GH, et al. Gene expression profile analysis to discover molecular signatures for early diagnosis and therapies of triple-negative breast cancer[J]. Front Mol Biosci, 2022, 9: 1049741.

[15] Tan RP, Cong T, Xu GW, et al. Anthracycline-induced atrial structural and electrical remodeling characterizes early cardiotoxicity and contributes to atrial conductive instability and dysfunction[J]. Antioxid Redox Signal, 2022, 37(1/2/3): 19-39.

[16] Leong DP, Lenihan DJ. Clinical practice guidelines in cardio-onco logy[J]. Heart Fail Clin, 2022, 18(3): 489-501.

[17] 高鹤,吴培香,肖利允,等.穴位刺激治疗冠心病心绞痛有效性和安全性的 meta 分析[J].中华全科医学,2023,21(4):698-703.
Gao H, Wu PX, Xiao LY, et al. Efficacy and safety of acupoint stimulation in the treatment of angina pectoris caused by coronary heart disease: a meta-analysis[J]. Chin J Gen Pract, 2023, 21(4): 698-703.

[18] 母晓艺,宋艳华,张蒂,等.针刺内关穴预处理改善心肌缺血再灌注损伤机制的研究进展[J].针灸临床杂志,2018,34(10):75-79.
Mu XY, Song YH, Zhang D, et al. Preconditioning of needling PC6 improving MIRI: a study of research progress[J]. J Clin Acupunct Moxibustion, 2018, 34(10): 75-79.

[19] 李晓陵,聂守萍,李昂,等.基于功能磁共振成像探究针刺内关穴治疗神志病证机制的研究进展[J].中国医药导报,2021,18(20):34-37.
Li XL, Nie SP, Li A, et al. Research progress on the mechanism of acupuncture at Neiguan in the treatment of mental disorders based on functional magnetic resonance imaging[J]. China Med Her, 2021, 18(20): 34-37.

[20] 林连枝,梁镇忠,陈嘉贤.指针内关穴治疗冠心病稳定型心绞痛的临床观察[J].中国医药导报,2010,7(22):126-128.
Lin LZ, Liang ZZ, Chen JX. Clinical observation on acupoint pointer in stable angina pectoris of coronary heart disease[J]. China Med Her, 2010, 7(22): 126-128.

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