

# Evaluation of the Preventive Effect of Regional Cooling Nursing on Hand Foot Syndrome Caused by Doxorubicin Hydrochloride Liposome

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## Abstract

**Purpose:** To explore the preventive effect of Regional cooling comprehensive nursing on hand foot syndrome caused by pegylated liposomal doxorubicin (PLD). **Method:** Adopt overall sampling method. Patients who used the same adjuvant drugs from January to December 2020 were randomly divided into an intervention group and a control group. The patients in the two groups received routine nursing guidance and drug prevention for the use of amygdalin. The patients in the intervention group were required to take protective measures of Regional cooling during chemotherapy. The occurrence of hand foot syndrome during adriamycin liposome administration was compared between the two groups. **Results:** By comparing the adverse reactions of cases during Adriamycin Administration, the incidence rates of grade I, II and III hand foot syndrome in the control group were 28.8%, 7.6% and 27.5% respectively, and the incidence rates of grade I, II and III hand foot syndrome in the intervention group were 42.1%, 12.3% and 7.0% respectively, with statistical significance ( $P < 0.05$ ). **Conclusion:** Regional cooling nursing and preventive behavior guidance can effectively reduce the severity of hand foot syndrome caused by adriamycin.

## Keywords

Hand-Foot Syndrome, Regional Cooling, Pegylated Liposomal Doxorubicin

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## 1. Introduction

Hand foot syndrome (HFS), also known as erythema palmaris and toes, is a kind of skin toxicity that occurs in tumor patients during chemotherapy or molecular targeted therapy. It is initially characterized by numbness, tingling or burning of the palms and soles. These symptoms usually occur at the same time as well-defined erythema with or without edema, cracking or peeling [1].

In the late stage, blisters and ulcers may appear. Volar and distal fat pads are often affected in front of the sole of the foot. The incidence rate of hand foot syndrome is 6% - 60.5% [2]. Although the occurrence of hand foot syndrome does not affect the life of patients, it can cause obvious discomfort and functional damage, and then affect the quality of life of patients [3]. Patients often feel that these changes make them cancer patients, and constantly remind them of their own diseases. Negative emotional experience is obvious, and they lack relevant disease knowledge and cognition [4].

In addition, these side effects may be discomfort or pain, limit normal daily functions, and leave permanent changes [5]. For grade III patients, it is often necessary to delay chemotherapy or reduce drug dose, or even change drugs.

Pegylated liposomal doxorubicin (PLD) is an anthracycline cytotoxic antibiotic. The incidence of hand foot syndrome in adjuvant treatment of breast cancer is 26.7% - 51.7% [6]. At present, in the research on the mechanism of HFS caused by drugs, the main reason is drug accumulation. Drugs penetrate into the skin and sweat glands from the capillaries of hands and feet, resulting in hand foot syndrome [7].

Preventing and managing skin toxicity associated with cancer treatment can minimize treatment interruptions and improve patient health. Awareness and early recognition are important for ensuring timely treatment and avoiding dose reduction or discontinuation of treatment. Effective measures to prevent and treat HFS include systemic and local treatment, dose reduction and switching to other similar drugs related to the low incidence of HFS. These methods allow patients to continue cancer treatment while reducing the negative impact on quality of life.

The existing prevention related studies are as follows: 1) Vitamin B6 has insufficient evidence support in preventing HFS, and its effect on reducing the risk of grade 2 and 3 HFS is controversial [8] [9] [10] [11] [12]; 2) Oral glucocorticoids or urea cream are the means of drug prevention [13]; 3) Effective nursing health education and patient support strategies are active and effective means of prevention and intervention [14], including avoiding hand foot stimulation, avoiding sunshine and hand foot thermal contact, and identifying early symptoms [15]. 4) It is reported in China that traditional Chinese medicine is more common in the treatment of HFS than in prevention [16] [17] [18].

Local ice compress and antiperspirant have also become the current measures to prevent HFS. Local ice compress restricts the circulation of drugs to the limbs by causing vasoconstriction, and reduces the accumulation of drug metabolites

in the palms and soles of the feet [19]. Some studies [20] found that local cooling measures were applied to prevent the occurrence of hand foot syndrome, or reduce the level of hand foot syndrome. However, there are still few studies on Chinese population samples. This study is mainly based on nursing guidance and clinical support, giving patients local hypothermia guidance and intervention. To explore the precautions and effects of local hypothermia nursing measures in the prevention of HFS caused by PLD.

## 2. Methods

### 2.1. Sample

Patients with breast cancer who visited the breast Department of a third-class hospital from January to December 2020. Inclusion criteria: 1) Pathological diagnosis of invasive breast cancer and knowledge of the condition; 2) Chemotherapy regimen contains liposome adriamycin; 3) There was no other heart, liver and kidney damage. Exclusion criteria: 1) have a history of tumors in other parts; 2) Have used chemotherapy drugs related to reported skin reactions; 3) Combined with other heart, liver and kidney damage; 4) Unable or refusing to use local hypothermia nursing measures due to physical conditions.

According to the time and conditions of admission, patients were divided into intervention group (57 cases) and control group (66 cases). There was no significant difference in patients' age, tumor stage, surgical method, chemotherapy regimen and adjuvant medication ( $P > 0.05$ ), which was comparable. See **Table 1** and **Table 2** for details.

**Table 1.** Comparison of general information and incidence rate of hand foot syndrome between the two groups.

Characteristics of All Patients (n = 123)		
Characteristics	Patients	%
<b>Age</b>		
<35	10	8.1
≥35	113	91.9
<b>BMI</b>		
Normal	69	56.1
Abnormal	54	43.9
<b>pT status</b>		
T1	49	39.8
T2	69	56.1
T3	5	4.1
<b>pN status</b>		
N0	56	45.5
N1	39	31.7
N2	14	11.4
N3	14	11.4

## Continued

<b>Stage</b>		
I	29	23.6
II	31	25.2
III	63	51.2
<b>Molecular subtyping</b>		
Luminal A	12	9.8
Luminal B	84	68.2
HER-2	12	9.8
TNBC	15	12.2
<b>Hand-foot syndrome</b>		
0	46	37.4
I	43	34.9
II	12	9.8
III	22	17.9

**Table 2.** Baseline characteristics of two groups of patients.

Baseline characteristics of two groups of patients			
	Intervention group (n = 57)	Control group (n = 66)	P value
<b>Age</b>			1.189
Median	49 (30 - 70)	47	
<35	7 (12.3)	3 (4.5)	
≥35	50 (87.7)	63 (95.5)	
<b>BMI</b>			2.246
Normal	36 (63.2)	34 (51.5)	
Abnormal	21 (36.8)	32 (48.5)	
<b>pT status</b>			0.048
T1	19 (33.3)	31 (47.0)	
T2	36 (63.2)	32 (48.5)	
T3	2 (3.5)	3 (4.5)	
<b>pN status</b>			0.087
N0	24 (42.1)	33 (50.0)	
N1	19 (33.3)	19 (28.8)	
N2	5 (8.8)	9 (13.6)	
N3	9 (15.8)	5 (7.6)	
<b>Stage</b>			0.284
I	12 (21.1)	17 (25.8)	
II	30 (52.6)	33 (50.0)	
III	15 (26.3)	16 (24.2)	
<b>Molecular subtyping</b>			0.014
Luminal A	6 (10.5)	6 (9.1)	
Luminal B	38 (66.7)	46 (69.7)	
HER-2	6 (10.5)	6 (9.1)	
TNBC	7 (12.3)	8 (12.1)	

## 2.2. Intervention Methods

Both groups received routine nursing guidance and education of liposomal adriamycin. During the four chemotherapy cycles of adriamycin liposome injection and within two months: 1) medication notification and psychological nursing. Inform patients of the advantages of the drug, infusion methods, adverse reactions and experience of effective prevention and treatment, reduce patients' fear and anxiety about chemotherapy, and improve compliance and confidence. 2) Avoid skin heat and light. Avoid exposing your skin to the sun when you go out. Physical sunscreen measures such as umbrellas and hats can be taken when the sun is intense; Avoid touching hot water and other objects with high temperature, and avoid soaking feet in hot water. 3) Avoid skin friction and irritation. Wear loose clothes, use soft wool towels, avoid chemical fiber fabrics, and choose soft shoes and socks. 4) Keep skin clean and moisturized. Those with sweaty hands and feet should be cleaned in time. In particular, keep feet clean and avoid accumulation of sweat on toes. Non irritating lotion can be used to prevent skin chapping and peeling. 5) Ensure vitamin intake. Maintain daily intake of vegetables, fruits and cereals. Avoid spicy food. 6) Early symptom recognition and active reporting. Timely detect the skin and sensory changes and tension at the finger tip. See a doctor in time when there is erythema, peeling, blisters or pain except pigmentation.

On this basis, the intervention group received local hypothermia nursing during drug metabolism. 1) Low temperature nursing during medication. Half an hour before intravenous infusion of liposomes, use medical ice bags for ice compress. Application site: it is used on the healthy side of the patient's upper limbs and feet. Precautions: pay attention to the patient's subjective feelings, and take it out in time if there is discomfort. Do not take a hot bath one hour before chemotherapy. 2) Low temperature nursing at home after medication. Soak hands and feet in cold water at normal temperature every day for 15 minutes each time. Stop in time if you feel unwell. Try to choose shoes that can keep the foot temperature low, or slippers, to avoid excessive warmth. If possible, you can choose a cooling package to cool your hands and feet. The medical ice bag is shown in **Figure 1**.



**Figure 1.** The medical ice bag.

### 2.3. Evaluation Method

The evaluation tool was based on the common toxicity standard for adverse reactions of the National Cancer Institute (NCI-CTCAE). The classification standard of hand foot syndrome can be divided into three levels: Level 1 is skin change or dermatitis, without pain; Grade 2 refers to painful skin changes (erythema or desquamation), but does not affect daily life and kinetic energy; Grade 3 refers to discomfort caused by painful skin changes (erythema or desquamation), which affects daily life or function.

### 2.4. Data Collection and Analysis

Data collection methods: patients were followed up at the beginning of the first chemotherapy. The incidence and degree of hand foot syndrome were followed up after 4 times of chemotherapy. The patients who have developed hand foot syndrome were tracked until the time of recovery. Hand foot syndrome and other adverse reactions of chemotherapy during 4 times of liposomal adriamycin chemotherapy were registered. Statistical methods were analyzed by SPSS18.0 software.

### 2.5. Ethics

This study was approved by Sun Yat-sen University Cancer Center IRB (NO.GYX2020-002).

## 3. Results

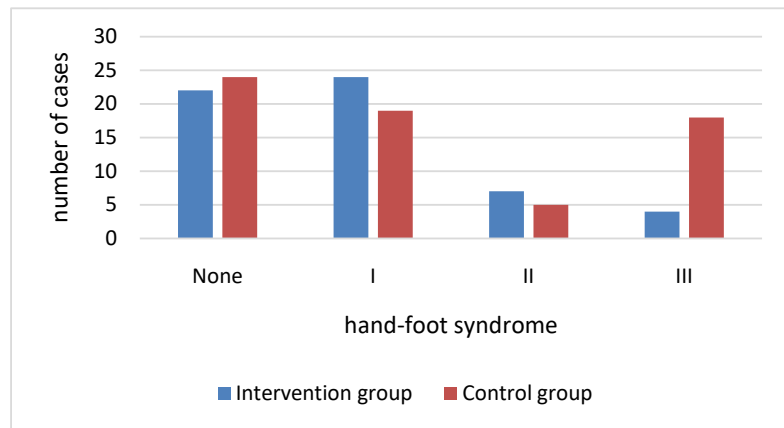
Through the analysis of the incidence of hand foot syndrome: the results showed that the incidence of the control group was 63.6%, and the incidence of the intervention group was 61.4%, the difference was statistically significant ( $P < 0.05$ ).

Through the mean value analysis of the classification of hand foot syndrome: the results show that there is no statistical difference between the control group and the intervention group.

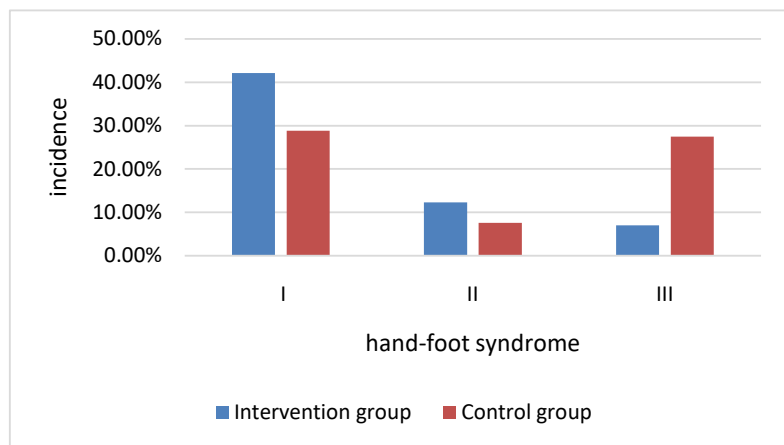
Through the incidence analysis of hand foot syndrome classification: the results are shown in **Figure 2** and **Figure 3**. The incidence rates of hand foot syndrome grade I, II and III in the control group are 28.8%, 7.6% and 27.5% respectively, and the incidence rates of hand foot syndrome grade I, II and III in the intervention group are 42.1%, 12.3% and 7.0% respectively, with statistically significant differences ( $\chi^2 = 9.264$ ,  $P < 0.05$ ). In addition, cases of hand foot syndrome grade I are mainly characterized by numbness of hands and feet and slight peeling; Grade II cases are mainly characterized by peeling of hands and feet and redness and swelling; Grade III cases are mainly characterized by numbness of hands and feet, moderate peeling, redness and swelling, and serious cases can have peeling and even blisters all over the body.

## 4. Discussion

Local hypothermia combined education support can reduce the risk of HFS



**Figure 2.** Number of cases of hand-foot syndrome in two groups.



**Figure 3.** Incidence of hand-foot syndrome in two groups.

Through this study, we can see that local hypothermia nursing can effectively reduce the risk of skin toxicity of hand foot syndrome after adriamycin liposome chemotherapy. The number of patients without hand foot syndrome increased significantly. The incidence of grade I, II and III decreased with statistical significance. There is also a relatively similar conclusion with similar studies: during treatment, using ice bags, ice water immersion or freezing gloves or socks to cool hands and feet has proved to be successful in reducing the incidence of HFS in cancer patients treated with PLD or docetaxel. A small prospective study of 53 gynecological cancer patients treated with PLD combined with carboplatin [21] showed that during PLD injection, the proportion of HFS at any level in patients treated with ice bags in the limbs was lower than that in patients without regional cooling (7% vs 36%;  $P = 0.01$ ).

However, local hypothermia nursing technology has not been implemented independently in this study or other studies. In addition to hypothermic nursing technology, we still need to do a good job in patients' prevention education and follow-up, early recognition of symptoms and intervention. Moreover, in this study, because vitamin B6 and oral glucocorticoids were not stopped, the role of

hypothermia nursing technology still needs further study.

Effective implementation methods and precautions of local hypothermia nursing technology

There is no clear and detailed intervention method and precautions of local hypothermia in the current study. According to the expert consensus on the management of adverse reactions of PLD (version 2020), the specific implementation of local ice compress is: when the patient is tolerant, use frozen gloves and socks ( $-22^{\circ}\text{C}$  refrigerator for 24 hours), and carry out local ice compress from 15 minutes before PLD chemotherapy to 15 minutes after the end of chemotherapy. Xie Tan *et al.* [20] studied by ice compress on the wrist and ankle at the beginning of chemotherapy until 30 min after PLD infusion. Mangili G's study [22] believes that the use of ice bags around the wrist and ankle is a simple and well tolerated prevention strategy. For patients receiving adriamycin liposomes, the incidence and severity of HFS can be significantly reduced by sticking ice bags on the wrist and ankle during the administration period. The incidence of HFS in the control group is 36%, while the incidence of HFS in the ice bag sticking group is 7.1%. The authors believe that the reduction of the incidence of HFS may play a role by inducing vasoconstriction and reducing the release of drugs in the limbs.

Generally, the recommended time for ice compress is 20 - 30 minutes, with an interval of 4 hours. The acceptability of patients and the prevention of adverse events such as frostbite should be taken into account in ice compress during administration. This study is based on the acceptability of patients to wash their hands and feet with cold water by using ice packs to compress their palms, wrists and ankles during chemotherapy and cold water to wash their hands and feet after chemotherapy. There are no special requirements for times and time. When using ice bags, wrap them uniformly with cotton pads to ensure that the ice bags do not directly contact the skin and prevent frostbite or pressure ulcers. Observe the skin of hands and feet during use and pay attention to the feelings of patients.

## 5. Limitation

In this study, the temperature controllable range of hypothermia nursing technology is not clear, and the clear time, tools, implementation methods, etc. in the implementation process of hypothermia nursing technology are not unified for patients. And the sample size is limited. In the future, it is necessary to improve the sample size range, formulate the prospective research of temperature range, and establish the norms and guidance of hypothermia nursing technology in the prevention of hand foot syndrome.

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## Statement of Ethics

This study was approved by Sun Yat-Sen University Cancer Center IRB (NO.GYX2020-002).

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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