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# Percutaneous nerve electrical stimulation for fatigue caused by chemotherapy for cervical cancer

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**Abstract**

This retrospective study investigated the effectiveness of percutaneous nerve electrical stimulation (PNES) for fatigue caused by chemotherapy for cervical cancer survivors.

Totally, 83 cases of fatigue caused by chemotherapy for cervical cancer survivors were analyzed. All these cases were assigned to a treatment group (n = 43), and a control group (n = 40). Patients in the treatment group received PNES, while the subjects in the control group were on waiting list. The treatment was applied once daily for a total of 6 weeks. The primary endpoint was fatigue. It was evaluated by the Multidimensional Fatigue Inventory (MFI), and Fatigue Questionnaire (FQ). The secondary endpoints consisted of anxiety and depression. They were measured by the Hospital Anxiety and Depression Scale (HADS). All outcomes were measured before and after 6-week treatment.

After treatment, PNES did not show significant difference in fatigue relief, measured by MFI (General fatigue, $P = .31$; Physical fatigue, $P = .44$; Activity, $P = .36$; Motivation, $P = .55$; Mental fatigue, $P = .49$), and FQ (Mental fatigue, $P = .29$; Physical fatigue, $P = .35$); and the reduction of anxiety and depression, measured by the HADS (Anxiety, $P = .21$; Depression, $P = .17$) after 6 weeks treatment between 2 groups.

This study demonstrated that PNES may not benefit for cervical cancer survivors with fatigue caused by chemotherapy after 6-week treatment.

**Abbreviations:** HADS = Hospital Anxiety and Depression Scale, MFI = Multidimensional Fatigue Inventory, PNES = percutaneous nerve electrical stimulation.

**Keywords:** cervical cancer, chemotherapy, fatigue, percutaneous nerve electrical stimulation

## 1. Introduction

Chemotherapy is utilized as 1 of the most common interventions for cancer treatment.[1–4] However, at the same time, it often brings a variety of side effects, such as fatigue, pain conditions, gastrointestinal reactions, and other tricky issues.[5–6] It has been reported that 50% to 75% patients receiving chemotherapy also experience fatigue.[7] The other study reported that rest and sleep alone can not help to alleviate this condition.[8] Moreover, if patients experienced this condition for a long time, it may result in anxiety, depression and poor quality of life.[9–10] Furthermore, very few treatment options can be utilized to treat cancer-related fatigue.

Complementary therapy, such as acupuncture, acupressure, massage, yoga, Chinese herbal medicine, and electrical stimulation is reported to treat chemotherapy-related fatigue.[11–17] Some other study also reported that such kinds of therapy can also help to relieve anxiety and depression, as well as the improvement of quality of life.[16] Of these, electrical stimulation, especially percutaneous nerve electrical stimulation (PNES) is 1 of the most potential candidates. However, current data is still insufficient to support that PNES can be utilized effectively to treat this condition. Therefore, in this retrospective study, we investigated the effectiveness and safety of PNES for the cervical cancer survivors with fatigue caused by chemotherapy.

## 2. Materials and methods

### 2.1. Design

A total of 83 cases of fatigue caused by chemotherapy for cervical cancer survivors were analyzed in this study. All these cases were selected between December 2015 and November 2017 from The Fourth People's Hospital of Shaanxi. All enrolled cases were assigned to a treatment group (n = 43) and a control group (n = 40). Subjects in the treatment group received PNES. The patients in the control group were on waiting list. The treatment period lasted a total of 6 weeks.

### 2.2. Ethical considerations

This retrospective study was approved by the Medical Ethical Committee of The Fourth People's Hospital of Shaanxi. This

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The authors have no conflicts of interest to disclose.

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study was conducted according to the Declaration of Helsinki. The informed consent form was waived from the enrolled patients because of the retrospective study.

### 2.3. Study population

All patient cases were selected from The Fourth People's Hospital of Shaanxi. The eligibility criteria for this retrospective study included patients aged from 21 to 75 years old with an International Federation of Gynecology and Obstetrics (FIGO) stage IIA-IVA. All participants had histological proven cervical cancer and were treated with chemotherapy. Patients with following conditions were excluded: pregnancy, breastfeeding, active psychiatric diseases, and medication-related fatigue. In addition, patients were also excluded if they had received electroacupuncture, electrical stimulation, and PNES 1 month before the study.

### 2.4. Treatment schedule

The patients in the treatment group were administered PNES by PNES device (HANS-100, Nanjing Jisheng Medical Technology Co., Ltd, Nanjing, China) at bilateral acupoints of Zusanli (ST36, 3 *cun* inferior to the bottom of the kneecap, 1 finger width lateral to the anterior crest of the tibia, in the tibialis anterior muscle), and Sanyinjiao (SP6, 3 *cun* directly superior to the tip of the medial malleolus on the posterior border of the tibia). It delivered frequency of 2 to 100 Hz for 30 minutes by 2 gel pads attached to a silicon patch at bilateral ST36 and SP6 respectively. The current intensity was gradually increased to the patient's maximum tolerance. Each patient was treated at each pair of points for 30 minutes, twice weekly for a total of 6 weeks. On the other hand, the patients in the control group were on waiting list during the period of 6-week treatment.

### 2.5. Outcome measurements

The primary endpoint was fatigue. It was measured by the Multidimensional Fatigue Inventory (MFI), each subscale ranges from 0 to 20, with lower scores indicating a lower degree of fatigue,[18] and Fatigue Questionnaire (FQ), consists of 11 items, each item varies from 0 to 3, a total score from 0 to 33, with 0 indicating better than usual, 3 indicating much worse than usual.[19] The secondary endpoints were anxiety and depression. They assessed by the Hospital Anxiety and Depression Scale (HADS) subscales, respectively.[20] Each item scores from 0 to 3, and a total score varies from 0 to 21 for either anxiety or depression. The higher score demonstrating more serious degree of the condition. All outcomes were evaluated before and after 6-week treatment.

### 2.6. Statistical analysis

All data were analyzed using SPSS software (SPSS V.17.0, IBM Corp., Armonk, NY). Mann–Whitney *U*-test was used for continuous non-normally data, while *t* test was utilized for normally variables. $\chi^2$ test or Fisher exact test was used to analyze the categorical data. $P < .05$ was set for the statistical significance.

## 3. Results

A total of 83 eligible cervical cancer survivors with fatigue caused by chemotherapy were included in this study. The characteristics of all included patients are listed in Table 1. The comparison of all these characteristic variables did not differ significantly between 2 groups.

**Table 1**

**Comparison of patient characteristics between 2 groups.**

| Variable | Treatment group (n = 43) | Control group (n = 40) | *P* value |
|---|---|---|---|
| Age (years) | 49.9 (11.7) | 52.2 (10.9) | .35 |
| Race (Asian China) | 43 (100.0) | 40 (100.0) | — |
| Marital status | | | |
| Single | 2 (4.7) | 1 (2.5) | .61 |
| Married | 37 (86.0) | 34 (85.0) | .89 |
| Divorced/widowed | 4 (9.3) | 5 (12.5) | .47 |
| Occupation | | | |
| Employed | 35 (81.4) | 33 (82.5) | .13 |
| Unemployed | 5 (11.6) | 5 (12.5) | .90 |
| Retired | 3 (7.0) | 2 (5.0) | .71 |
| FIGO performance status | | | |
| IIA | 4 (9.3) | 3 (7.5) | .77 |
| IIB | 15 (34.9) | 13 (32.5) | .82 |
| IIIA | 17 (39.5) | 14 (35.0) | .67 |
| IIIB | 5 (11.6) | 7 (17.5) | .45 |
| IVA | 2 (4.7) | 3 (7.5) | .59 |
| Chemotherapy | | | |
| Fluorouracil | 17 (39.5) | 18 (45.0) | .61 |
| Carboplatin | 24 (55.8) | 22 (55.0) | .94 |
| Other | 6 (14.0) | 5 (12.5) | .85 |
| Hemoglobin (g/dL) | 12.3 (1.8) | 12.5 (1.5) | .41 |
| Albumin (g/dL) | 4.0 (0.2) | 4.1 (0.4) | .15 |

Data are present as mean ± standard deviation or number (%). FIGO = International Federation of Gynecology and Obstetrics.

Before treatment, there were no significant differences in fatigue, measured by (General fatigue, $P = .33$; physical fatigue, $P = .26$; activity, $P = .77$; motivation, $P = .64$; mental fatigue, $P = .64$; Table 2), and FQ (mental fatigue, $P = .56$; physical fatigue, $P = .46$; Table 2); and anxiety and depression, assessed by HADS sub-scales respectively (anxiety, $P = .65$; depression, $P = .67$; Table 2) between 2 groups.

After treatment, patients in the treatment group did not show greater improvement, neither in fatigue, measured by MFI (general fatigue, $P = .31$; physical fatigue, $P = .44$; activity, $P = .36$; motivation, $P = .55$; mental fatigue, $P = .49$; Table 3),

**Table 2**

**Comparison of outcome measurements before the treatment between 2 groups.**

| Outcome measurements | Treatment group (n = 43) | Control group (n = 40) | *P* value |
|---|---|---|---|
| MFI scale | | | |
| General fatigue | 13.4 (2.2) | 12.9 (2.5) | .33 |
| Physical fatigue | 12.8 (1.9) | 12.3 (2.1) | .26 |
| Activity | 12.1 (3.3) | 11.9 (3.0) | .77 |
| Motivation | 11.6 (3.7) | 11.2 (4.1) | .64 |
| Mental fatigue | 13.0 (2.8) | 12.7 (3.2) | .65 |
| FQ | | | |
| Mental fatigue | 8.1 (1.6) | 7.9 (1.5) | .56 |
| Physical fatigue | 8.5 (1.7) | 8.2 (2.0) | .46 |
| HADS | | | |
| Anxiety | 7.5 (2.7) | 7.2 (3.2) | .65 |
| Depression | 7.3 (3.1) | 7.0 (3.3) | .67 |

Data are present as mean ± standard deviation or number (%). FQ = Fatigue Questionnaire, HADS = Hospital Anxiety and Depression Scale, MFI = Multidimensional Fatigue Inventory.

**Table 3**

**Primary outcome measurements after treatment (change from baseline).**

| Fatigue | Treatment group (n = 43) | Control group (n = 40) | Difference | *P* value |
|---|---|---|---|---|
| MFI | | | | |
| General fatigue | −2.3 (−3.2, −1.5) | −0.7 (−1.5, −0.2) | −1.6 (−2.2, −1.0) | .31 |
| Physical fatigue | −1.8 (−2.5, −1.0) | −0.5 (−0.9, 0.2) | −1.3 (−-1.9, −0.7) | .44 |
| Activity | −2.5 (−3.4, −1.6) | −1.0 (−1.7, −0.4) | −1.5 (−2.1, −0.8) | .36 |
| Motivation | −1.5 (−2.2, −0.7) | −0.5 (−1.0, −0.2) | −1.0 (−1.4, −0.5) | .55 |
| Mental fatigue | −1.7 (−2.6, −0.9) | −0.4 (−0.8, −0.1) | −1.2 (−1.7, −0.7) | .49 |
| FQ | | | | |
| Mental fatigue | −1.1 (−1.7, −0.4) | −0.3 (−0.8, −0.1) | −0.8 (−1.2, −0.4) | .29 |
| Physical fatigue | −1.2 (−1.9, −0.6) | −0.5 (−1.1, −0.1) | −0.7 (−1.1, −0.3) | .35 |

Data are present as mean (range). FQ = Fatigue Questionnaire, MFI = Multidimensional Fatigue Inventory.

**Table 4**

**Secondary outcome measurements after treatment (change from treatment before).**

| HADS | Treatment group (n = 43) | Control group (n = 40) | Difference | *P* value |
|---|---|---|---|---|
| Anxiety | −1.9 (−3.1, −1.0) | −0.9 (−1.6, −0.3) | −0.9 (−1.5, −0.4) | .21 |
| Depression | −1.3 (−1.8, −0.5) | −0.5 (−1.1, −0.1) | −0.7 (−1.1, −0.3) | .17 |

Data are present as mean (range). HADS = Hospital Anxiety and Depression Scale.

and FQ (mental fatigue, $P = .29$; physical fatigue, $P = .35$; Table 3); nor in anxiety and depression, evaluated by HADS (Anxiety, $P = .21$; depression, $P = .17$; Table 4), compared with patients in the control group.

After treatment, no any kinds of adverse events were recorded in this retrospective study. No treatment-related death occurred in either group.

## 4. Discussion

In China, many physicians utilized the electrical stimulation to treat fatigue, especially the cancer survivors with fatigue caused by chemotherapy widely. This kind of therapy includes neuromuscular electrical stimulation, transcutaneous electrical stimulation, PNES, and even the electroacupuncture. However, there are still limit available data and few convinced evidence can support this therapy, especially for the PNES.

To our best knowledge, the present study is the first study to explore the effectiveness and safety of PNES for the treatment of cervical cancer survivors with fatigue caused by chemotherapy. The results of this study may provide the helpful evidence for the clinical practice, as well as the potential clues for the further study.

The results of this study demonstrated that although no adverse events occurred in the either group, patients in the treatment group did not exert better outcomes in fatigue relief, as measured by MFI and FQ; and anxiety and depression, as assessed by the HADS after 6 weeks treatment, compared with patients in the control group. The results indicated that PNES may be not efficacious for cervical cancer survivors with fatigue resulted from chemotherapy after 6 weeks treatment.

This retrospective study suffered from 3 following limitations. First, this study did not involve randomization and blinding procedure, which may cause high risk of selection.[21] Second, the dose of PNES may be insufficient in this study, which may account for the negative results of this study. Third, the sample size is quite small, which may also affect the results of this study. Therefore, further studies should avoid these limitations.

## 5. Conclusion

The results of this study found that PNES may be not efficacious for cervical cancer survivors with fatigue caused by chemotherapy after 6 weeks treatment.

## Author contributions

**Conceptualization:** Xiang-zhuan Gao, Ting Fu, Hui-juan Guang.
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