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Effect of neuromuscular electrical stimulation for fatigue management in patients with advanced laryngeal cancer receiving chemoradiotherapy

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Abstract

This study retrospectively investigated the effect of neuromuscular electrical stimulation (NMES) for fatigue management in patients with advanced laryngeal cancer (ALC) receiving chemoradiotherapy.

A total of 60 eligible patients with ALC receiving chemoradiotherapy were included. These patients were assigned equally to a treatment group and a control group. Patients in the treatment group received NMES therapy and were treated for a total of 8 weeks, while the patients in the control group did not receive NMES therapy. The primary outcome was fatigue, measured by the multidimensional fatigue inventory (MFI). The secondary outcomes included anxiety and depression, measured by the Hospital Anxiety and Depression Scale (HADS), and sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI). All outcomes were evaluated before and after 8-week NMES treatment

After 8-week NMES treatment, the patients in the treatment group did not exert better effect than patients in the control group in fatigue relief, measured by the MFI score, anxiety and depression decrease, assessed by HADS, and sleep quality improvement, evaluated by PSQI.

The results of this study demonstrate that NMES may not benefit for fatigue relief in patients with ALC receiving chemoradiotherapy. Future studies should still focus on this topic and warrant these results.

Abbreviations: ALC = advanced laryngeal cancer, HADS = Hospital Anxiety and Depression Scale, LC = laryngeal cancer, MFI = multidimensional fatigue inventory, NMES = neuromuscular electrical stimulation, NSCLC = nonsmall cell lung cancer, PSQI = Pittsburgh Sleep Quality Index, TEAS = transcutaneous electrical acupoint stimulation.

Keywords: advanced laryngeal cancer, effect, neuromuscular electrical stimulation

1. Introduction

Laryngeal cancer (LC) is one of the most common types of malignant tumors for human being.[1–3] It has been reported that surgical treatment may be effective for patients with early LC.[4,5] However, patients are often difficult to achieve the desired results with advanced laryngeal carcinoma (ALC).[6,7]

Chemoradiotherapy is a primary intervention for the ALC, and it is reported that patients have 10% to 45% of 5-year overall survival.[8–10] Unfortunately, most patients receiving chemoradiotherapy often experience a variety of adverse effects.[11–13] These adverse effects often consist of fatigue, anemia, leukopenia, thrombopenia, nausea, vomiting, diarrhea, stomatitis, infection, and renal and hepatic toxicity.

Previous study reported that about 50% to 75% patients with cancers had experienced fatigue when they received such treatment.[14] It is also reported that such number increases to 80% to 96% for patients with cancer undergoing chemotherapy, and 60% to 93% for them also receiving radiotherapy.[15,16] Additionally, such condition can also result in anxiety, depression, and a very poor quality of life for those patients.[17,18] Unfortunately, very few interventions can effectively manage the condition of cancer-related fatigue.

Complementary and alternative therapy is reported to treat such condition effectively.[19,20] These interventions include acupuncture, acupressure, massage, moxibustion, yoga, Qigong, Tai Chi, and neuromuscular electrical stimulation (NMES).[21–30] Of those, NMES is one of the most potential management for decreasing cancer-related fatigue. However, no data is available to support that NMES can effectively manage this condition, especially specific in patients with ALC. Thus, in this retrospective study, we explored the potential effect of NMES for managing treatment-related fatigue in patients with ALC receiving chemoradiotherapy.

2. Methods and patients

2.1. Ethics

This study was approved by the Ethical Committees of First Affiliated Hospital of Jiamusi University, Second Affiliated Hospital of Jiamusi University, and Hongqi Affiliated Hospital of Mudanjiang Medical University. All patients provided signed informed consent in this study.

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M-jZ and J-wM contributed equally to this study.

The authors have no conflicts of interest to disclose.

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2.2. Design

This retrospective study was conducted between June 2016 and October 2017 at First Affiliated Hospital of Jiamusi University, Second Affiliated Hospital of Jiamusi University, and Hongqi Affiliated Hospital of Mudanjiang Medical University. It included 60 eligible patients with ALC receiving chemoradiotherapy. Of these patients, 30 patients in the treatment group received NMES, while the other 30 patients did not receive this intervention.

2.3. Participants

All patients aged between 18 and 70 years old were histologically confirmed diagnosis of ALC with squamous cell carcinoma. Additionally, patients were also needed to meet the clinical stages of III and IV diseases, according to the Union for International Cancer Control,[31] as well as the locations of all tumors in the glottis or supraglottis. Patients were excluded if they had cardiology diseases, metal embedded into the body around the utilized points, abnormal functions of liver and kidney, severe systemic complications, mental disorder, and gestational or lactating. In addition, the patient cases were also excluded if they had incomplete data, and received therapies of electrical stimulations, such as NMES, electroacupuncture, and any others.

2.4. Management

All patients in the treatment group were administered NMES using NMES device (HANS-100, Nanjing Jisheng Medical Technology Co, Ltd, Nanjing, China) with a frequency of 2 to 100 Hz, at bilateral Zusanli (ST36),[32] 30 minutes each session, 1 session daily, 2 sessions weekly for a total of 8 weeks. The current intensity was gradually increased to the maximum tolerance of each individual subject. ST36 locates 3 *cun* below the lower border of the patella, and 1 finger width lateral from the anterior border of the tibia. The patients in the control group did not receive NMES treatment during the period of fatigue management with NEMS in the control group.

2.5. Outcomes

The primary outcome included fatigue, measured by the multidimensional fatigue inventory (MFI).[33] It included 5 subscales, each scale varies from 0 to 20, with the lower score indicating the less degree of fatigue. The secondary outcomes consisted of anxiety and depression, measured by the Hospital Anxiety and Depression Scale (HADS),[34] and sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI).[35] The HADS scale consists of an anxiety subscale and a depression subscale, with 7 items in both subscales. Each scale rates from 0, best status, to 3, worst status. The PSQI scale ranges from 0 to 21, with a lower score denoting a better sleep quality. All outcomes were evaluated before and after 8-week NMES treatment.

2.6. Statistical analysis

All baseline and outcome data were analyzed by using SAS package 8.2 (SAS Institute Inc, Cary, NC). Continuous data was analyzed by the *t* test or Mann–Whitney rank sum test. Categorical data was analyzed by the Pearson χ^2 test or Fisher exact test. $P < .05$ was set as the statistical significance level.

3. Results

The characteristics of all 60 eligible patients with ALC are summarized in this retrospective study (Table 1). There were not significant differences in all characteristics between 2 groups before the study.

After 8-week NMES treatment, patients in the treatment group neither showed better outcomes in cancer-related fatigue relief, as measured by MFI scale (general fatigue, $P = .21$; physical fatigue, $P = .33$; activity, $P = .15$; motivation, $P = .24$; mental fatigue, $P = .64$; Table 2), nor the anxiety ($P = .23$, Table 3) and depression ($P = .38$, Table 3) relief, assessed by the HADS scale, as well as the sleep quality improvement, evaluated by the PSQI scale ($P = .59$, Table 3).

Table 1

Characteristics of all included patients at baseline.

Characteristics	Treatment group (n = 30)	Control group (n = 30)	*P* value
Age, y	64.2 (9.8)	63.9 (10.6)	.91
Gender			
Male	21 (70.0)	17 (56.7)	.29
Female	9 (30.0)	13 (43.3)	.29
Race (Han ethnicity)	30 (100.0)	30 (100.0)	1.00
Marital status			
Married	24 (80.0)	26 (86.7)	.49
Divorced/widowed	6 (20.0)	4 (13.3)	.49
Performance status			
0	10 (33.3)	13 (43.3)	.43
1	20 (66.7)	17 (56.7)	.43
Location			
Supra glottis	14 (46.7)	15 (50.0)	.80
Vocal cord	16 (53.3)	15 (50.0)	.80
T category			
T1	2 (6.7)	3 (10.0)	.64
T2	4 (13.3)	2 (6.7)	.40
T3	18 (60.0)	21 (70.0)	.42
T4	6 (20.0)	4 (13.3)	.49
N category			
N0	23 (76.7)	21 (70.0)	.56
N1	2 (6.7)	3 (10.0)	.64
N2	4 (13.3)	4 (13.3)	1.00
N3	1 (3.3)	2 (6.7)	.56
Disease stage			
III	18 (60.0)	20 (25.0)	.59
IV	12 (40.0)	10 (25.0)	.59
MFI scale			
General fatigue	17.4 (3.0)	17.1 (3.1)	.70
Physical fatigue	16.1 (2.9)	16.3 (2.6)	.78
Activity	14.8 (3.0)	15.0 (3.2)	.80
Motivation	13.3 (3.7)	13.5 (3.9)	.84
Mental fatigue	14.2 (3.1)	14.5 (3.4)	.72
HADS-Anxiety	6.9 (2.9)	7.0 (3.1)	.90
HADS-Depression	7.2 (3.3)	7.1 (3.1)	.90
PSQI-Sleep quality	9.0 (3.7)	8.8 (4.0)	.84
Radiotherapy	30 (100.0)	30 (100.0)	1.00
Chemotherapy			
Cisplatin	15 (50.0)	10 (33.3)	.19
Fluorouracil	11 (36.7)	7 (23.3)	.26
Capecitabine	6 (20.0)	8 (26.7)	.54
Carboplatin	4 (13.3)	5 (16.7)	.72
Paclitaxel	4 (13.3)	3 (10.0)	.69
Gemcitabine	3 (10.0)	4 (13.3)	.69

Note: Data are present as mean ± standard deviation or number (%). HADS = Hospital Anxiety and Depression Scale, MFI = Multidimensional Fatigue Inventory, PSQI = Pittsburgh Sleep Quality Index.

Table 2

Primary outcome measurement after 8-wk treatment (change from before treatment).

Fatigue	Treatment group (n = 30)	Control group (n = 30)	Difference	*P* value
General fatigue	−1.6 (−2.5, −0.9)	−0.8 (−1.6, −0.2)	−0.8 (−1.3, −0.3)	.21
Physical fatigue	−1.3 (−2.1, −0.5)	−0.6 (−0.9, −0.1)	−0.6 (−1.0, −0.2)	.33
Activity	−1.7 (−2.6, −1.1)	−0.7 (−1.2,−0.1)	−0.9 (−1.5, −0.4)	.15
Motivation	−1.2 (−1.8, −0.4)	−0.5 (−0.9, −0.2)	−0.7 (−1.2, −0.4)	.24
Mental fatigue	−0.9 (−1.7,−0.4)	−0.3 (−0.8, −0.1)	−0.5 (−0.8,−0.2)	.64

Note: Data are present as mean ± standard deviation.

Table 3

Secondary outcome measurement after 8-wk treatment (change from before treatment).

Outcome measurements	Treatment group (n = 30)	Control group (n = 30)	Difference	*P* value
Anxiety				
HADS-Anxiety	−1.3 (−2.1,−0.5)	−0.5 (−1.1, −0.2)	−0.8 (−1.2,−0.4)	.23
Depression				
HADS-Depression	−1.1 (−1.6,−0.4)	−0.4 (−0.9, −0.1)	−0.7 (−1.1, −0.3)	.38
Sleep quality				
PSQI	−1.0 (−1.7, −0.5)	−0.4 (−0.8,−0.2)	−0.5 (−0.8, −0.2)	.59

Note: Data are present as mean ± standard deviation.
HADS = Hospital Anxiety and Depression Scale, PSQI = Pittsburgh Sleep Quality Index.

4. Discussion

Previous related study explored the effectiveness of transcutaneous electrical acupoint stimulation (TEAS) therapy on cancer-related fatigue in patients with nonsmall cell lung

cancer (NSCLC) after chemotherapy.[29] It found that chemotherapy may increase the fatigue in patients with NSCLC. Fortunately, TEAS can help relive cancer related fatigue in those patients.[29]

Currently, no clinical study has explored the effect of NMES for managing treatment-related fatigue in patients with ALC receiving chemoradiotherapy. To the best of our knowledge, this study first investigated the effect of NMES for fatigue relief in patients with ALC undergoing chemoradiotherapy. The results of this study were inconsistent with the previous related study.[29]

The results of this first retrospectively study showed that NMES did not demonstrate promising outcomes in cancer-related fatigue relief, measured by MFI; anxiety and depression decrease; and sleep quality improvement in patients with ALC receiving chemoradiotherapy. It indicates that NMES may not benefit for cancer-related fatigue management in patients with ALC.

This study has several limitations. First, this study is a retrospective study, all the outcome data were just based on the current available data. Thus, no comprehensive outcome measurements were included in this study, such as outcome evaluation of voice rehabilitation. Second, the sample size in this study is quite small, which may affect the results of this study. Third, this study just assessed the outcome measurements after 8-week treatment, and no follow-up evaluations were utilized after the treatment. Thus, future studies should avoid the above limitations for further focus on this issue.

5. Conclusion

The results of this study demonstrated that NMES may not benefit the fatigue relief in patients with ALC receiving chemoradiotherapy.

Author contributions

Conceptualization: Wei Zhao, Mei-jia Zhang, Xiu-sheng Qu, Chong Feng.
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