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Original Article

Acupoint stimulation improves pain and quality of life in head and neck cancer patients with chemoradiotherapy: A randomized controlled trial

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ABSTRACT

Objective: This study aimed to evaluate the effect of acupoint stimulation on pain, negative moods, and quality of life for head and neck cancer (HNC) patients who underwent concurrent chemoradiotherapy (CCRT).
Methods: This randomized controlled trial recruited participants from a medical center and randomly assigned using a permuted block randomization list with computer-generated random serial numbers into the AcuCare group ($n = 46$) receiving acupoint stimulation with transcutaneous acupoint electrical stimulation (TAES) and auricular acupressure (AA) or the control group ($n = 46$) without any acupoint stimulation. Outcomes were repeatedly assessed pain intensity using the visual analogue scale, negative moods using the hospital anxiety and depression scale, and quality of life (QoL) using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Head and Neck 35.
Results: After adjusting varying mucositis grades and time-dependent growth effects, the generalized estimating equations showed a significantly increase in pain intensity at weeks 1, 2, 3, and 6 ($P < 0.05$), but not in negative moods ($P > 0.05$), compared to baseline and control group. Analysis of covariance showed a significant group-difference in the senses problems of QoL ($F = 7.33$, $P = 0.01$) at Week 6.
Conclusions: This study supports that acupoint stimulation could effectively reduce pain and improve senses problem of QoL for patients with HNC.
Trial registration: This study was registered at https://clinicaltrials.gov/NCT03640195.

Introduction

Head and neck cancer (HNC) encompasses malignancies of the upper aerodigestive tract with a larger area involving lip, oral cavity, larynx, nasopharynx, oropharynx, hypopharynx, and salivary glands. The incidence and mortality of HNC is worldwide estimated to be 887,000 and 453,000 people, respectively.[1] In Taiwan, in a population of estimated 23,000,000 people, HNC accounts for more than 13,000 newly diagnosed cases and over 4300 deaths.[2] To treat HNC patient therapeutic modalities comprise surgery, radiotherapy, and chemotherapy.[3] In particular, chemotherapy combined with radiotherapy in treating cancer patients is recommended.[4] However, concurrent chemoradiotherapy (CCRT) exacerbates the severity and interference of symptoms,[5] negatively influences psychological impact and quality of life (QoL).[6] Therefore to address CCRT induced symptoms not only relieve pain but also negative moods and QOL.

Given oncological therapy, over 60% of HNC patients suffered moderate to severe pain with mucositis and dermatitis in oral and cervicofacial regions,[7] especially those treated by CCRT treatment.[8] In HNC patients with CCRT, the incidence of mucositis (grades 3 and 4) and dermatitis was 33% and 41%, respectively.[9] With increasing cumulative therapeutic dose, oral pain was experienced[10] and ulcerative lesions gradually worsened.[11] A study pointed out that HNC patients received CCRT required analgesia and over 80% of them required opioids.[12] However, the effect of opioids in relieving HNC or mucositis pain is less[13] and side effects were concerned.[14] Healthcare professionals and cancer patients increasingly seek non-pharmacological treatment alone or combined with conventional therapy for managing cancer-related pain.[15] Stimulating acupoint can alleviate pain through rectify body energy (qi) and blood circulation to restore homeostasis according to the principles of traditional Chinese medicine.[16]

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Pain not only causes treatment disruption but it also impacts QoL,[12] interfering with physical functions,[17] such as eating, swallowing, and verbal communication.[18] Previous studies indicated that CCRT-induced side effects were associated with negative emotional symptoms such as depression and anxiety,[19] which resulted in reducing HNC patients' QoL,[20] vice versa, reduced QoL worsened anxiety and depression.[21] Unfortunately, emotional symptoms also increased HNC patients' risk of treatment interruption.[22] Therefore, to address CCRT-induced symptoms not only relieve pain but also negative moods and QoL.

Transcutaneous electrical acupoint stimulation (TAES) is one of acupuncture-related techniques stimulated acupoints to produce acupuncture-like effects, and applying it has shown promising effects in pain management.[23] TAES and acupuncture was beneficial in relieving pain,[24,25] and improving anxiety,[26,27] depression[28] and QoL.[25,26] However, a systematic review revealed that acupuncture improved QoL but it failed to relieve depressive symptoms.[29] The other systematic review confirmed that acupuncture was effective in relieving cancer-related pain, but not chemotherapy- or radiotherapy-induced pain.[30] Although TAES is studied in intervention effects as not many as acupuncture does, it is non-invasive modality that may reduce needle fear from patients and promote their favorable psychological effects. In addition to TAES, auricular acupressure (AA) is a non-invasive acupoint stimulation and achieves acupuncture-like effects through the pressing of taped seeds and fingers. A number of systematic review reported that acupressure and acupuncture when combined with pharmacological therapy alleviated pain,[31–33] reduced opioid dose,[31] shorter analgesic onset time[33] or onset time of pain relief,[32] longer pain-free duration,[32,33] and improved QoL.[32] As auricular acupuncture alone, it lowered acute pain intensity and duration, and shortened the duration of acute mucosal toxicity in HNC patients receiving chemoradiotherapy.[34] Auricular acupuncture also reduces the use of analgesics effectively.[35] Notably, auricular therapy is a favored acupressure, followed by acupuncture.[36] In cancer patients, auricular acupoints stimulation is effective in relieving pain,[37] anxiety, depression,[38] and QoL.[39] However, insufficient evidence to determine the effect of acupuncture-related techniques in relieving cancer pain was concluded according to a Cochrane systematic review.[40] To address the gap in knowledge and determine the effect of a non-invasive intervention, this study aimed to evaluate the effect of acupoint stimulation on pain intensity, negative moods, QoL for HNC patients who underwent CCRT.

Methods

Design and participants

This randomized controlled trial comprised two groups and five repeated-measures. Participants were recruited from a radiation outpatient at a medical center in northern Taiwan. The participants included were randomly assigned to the AcuCare group that received routine care and acupoint stimulation with TAES and AA, whereas the control group received routine care only. The outcomes of pain intensity, negative moods, and QoL were measured. Data were collected for pain intensity and negative moods before intervention as the baseline, weeks 1, 2, 3, and 6 during the intervention period, and for QoL at baseline and Week 6. Patients who were aged 20 years or more, diagnosed with HNC, treated by CCRT, and communicable were included. For participants treated by radiotherapy, but with history of arrhythmia, pacemaker usage, or lesion on the selected acupoints were excluded. The sample size was estimated by the primary outcome of pain intensity in HNC patients and calculated by using the software G Power 3.1.2. An estimated effect size of 0.24 based on the previous study[27] at a 5% level of significance with 80% power and five repeated measures, 84 participants were minimally required. With a considered 10% of the attrition rate, 92 (46 in each group) were to be necessary. Figure 1 represents the research design and participant allocation.

Randomization

The process of randomization and concealment allocation was conducted by a research team who were not involved in the study. A random allocation software used a permuted block randomization with a block of four to ensure an equal number in each group, and random numbers were sequentially sealed in a continuously numbered and opaque envelope. The envelopes were opened sequentially to allocate participants to the AcuCare or control group by the other researcher. Because of the nature of acupoint stimulation intervention, it was not possible to blind the participants about the intervention.

Interventions

The acupoint stimulation intervention involved two parts, including TAES and AA. The acupoints of *hegu* (LI4) and *lieque* (LU7) were selected and stimulated by TAES (Figure 2). LI4 is categorized into the large intestine meridian and located on the dorsum of the hand, radial to the midpoint of the second metacarpal.[41] LI4 can stop the pain through regulating defensive qi and tonifying qi flow to remove obstructions from the channel.[16] LU7 is categorized into the lung meridian, and located on the radial aspect of the forearm, between the tendons of the abductor pollicis muscles, in the groove for the abductor pollicis longus tendon and 1.5 B-cun superior to the palmar wrist crease.[41] LU7 can neuropathic pain and dry throat symptoms of head and neck diseases through regulating defensive qi and releasing to expel exterior wind-cold or heat.[16] TAES was applied to a transcutaneous nerve electrical stimulation device (Model-05B, Ching Ming Tens, Taiwan) with two pairs of disposable electrode pads (1 × 1 cm) at the unilateral of LI4 and LU7 (left hand first) for 20 min in one section. The dense-and-dispersed stimulation waveform was delivered alternating pulses of 10 Hz and 80 Hz; a current output of 4–7 mA was adjusted depending on the individual's tolerance.[42]

In each section of intervention, followed by TAES, auricular acupressure was applied to prolong stimulation onto *shenmen* (TF4), *mouth* (IC6), *subcortex* (AT5), and *occiput* (AT3) (Figure 2). TF4 is located in the lateral angu area of the triangular fossa. Given the pressure to the TF4, it raises endorphin levels to reach sedative and analgesic effects.[43] IC6 is located in the cavum concha area. Given the pressure to the IC6, it has analgesic for reducing oral pain.[43] AT5 is located on the anterior surface of the inner wall of the antitragus, and AT3 is located on the posterior, superior part of the antitragus, which normalizes qi energy flow and harmonizes the cerebral cortex.[44] Wangbuliuxingzi seeds (Beijing, China) was used and placed with an adhesive patch onto the unilateral each selected auricular acupoint (left ear first). Participants were instructed to press each acupoint by thumb and index finger for 1 min, three times a day, five days a week, and remove the taped seeds on the sixth day. They were noted that they experienced various sensations while pressing, including numbness, swelling, mild pain, or warmth. Seeds were taped on the other side of the ear weekly, and participants' accuracy and compliance in their AA performance were also checked weekly. To ensure each participant's accuracy and compliance, an instructional booklet was provided to each participant; the booklet consisted of the main contents of illustration of auricular acupoint location, direction of auricular acupressure operation, explanation of sensations while pressing, and precautions of auricular pressure reactions. Participants were also asked to record daily their performance, sensations and reactions from pressing auricular acupoints in the pamphlet with date and checkmarks.

The TAES and AA interventions were given six sections, once a week for six weeks, by well-trained researcher nurses. One TCM physician and one TCM nurse verified the conduct of the TAES and AA, which consisted of a selection of acupoints, current frequency and output, waveform, and length of stimulation. In addition, all participants received the same routine care that was general radiation therapy care and medications for pain management provided by the study hospital professionals. Prior to

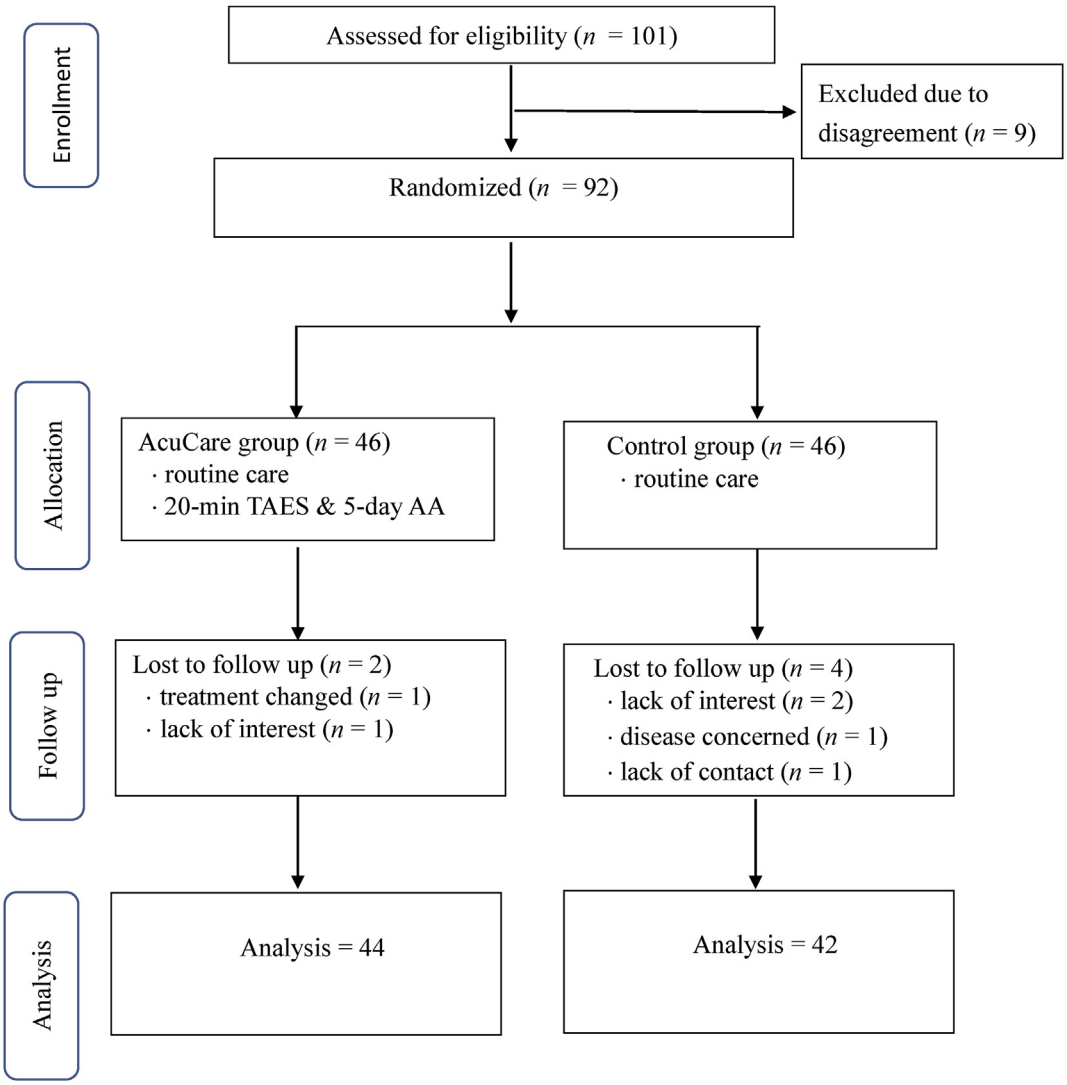

Figure 1. The flowchart of the research design and participant allocation. Note: TAES, Transcutaneous acupoint electrical stimulation; AA, Auricular acupressure; HADS, Hospital anxiety and depression scale; EORTC QLQ-H&N 35, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Head and Neck 35.

the study, every participant was assessed by the radiation oncologists and identified as being appropriate and safe. In addition, the TAES and AA interventions were performed after radiation therapy for the participants in the AcuCare group. Data collection was conducted by the same two researcher nurses at baseline, weeks 1, 2, 3, and 6.

Measures

Pain intensity was the primary outcome, whereas negative moods, quality of life were the secondary outcomes. Demographic characteristics were also collected, including age, gender, education, smoking, drinking, Betel quid history; clinical characteristics include, tumor site and stage, surgery, oral mucositis grade, a chemotherapy drug, and radiotherapy total dose. Pain intensity was measured by using the visual analogue scale (VAS) to assess a change in pain perception in patients maintaining medical therapy. The VAS consisted of a 10-cm straight line with ranging from 0 cm (no pain) to 10 cm (extreme pain). Participants marked their pain level on the line between the two endpoints. The distance between 0 cm and the mark then defined participants' pain. A cut-off point was suggested (0–0.4 cm = no pain; 0.5–4.4 cm = mild pain; 4.5–7.4 cm = moderate pain; 7.5–10 cm = severe pain). The retest reliability of the VAS confirmed across time points.[45]

Negative moods were measured by using the hospital anxiety and depression scale (HADS), which was developed by Zigmond and Snaith to assess both anxiety and depression, which commonly coexist in response to stressors.[46] This questionnaire consisted of 14 items and categorized into the subscales of anxiety and depression. The responses were rated on a scale from 0 to 3 for each item. A total score ranged from 0 to 42, with a higher score representing more severe negative moods, and a score of more than 14 indicating clinically significant emotional distress.[47] Cronbach's α of the HADS was 0.88 in this study. Additionally, QoL was measured by using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Head and Neck 35 (EORTC QLQ-H & N 35) that was developed by the European Organization for Research and Treatment of Cancer and designed to assess HNC-specific quality of life.[48] This questionnaire consisted of 35 items and divided into the seven symptom subscales that were pain, swallowing, senses problems, speech problems, trouble with social eating, trouble with social contact, and less sexuality. Each item was scored on a four-point Likert scale (1 = not at all; 2 = a little; 3 = quite a bit; 4 = very much), and then linearly transformed to a 0–100 point. A higher score indicated worse symptoms. Cronbach's α of seven subscales of the EORTC QLQ-H & N 35 was between 0.70 and 0.98 in this study.

Data analysis

All statistical analyses were performed using SPSS 20.0 for Windows (IBM Corp., Armonk, NY, USA). Data were analyzed by a researcher who was not involved in the study. Descriptive statistical analysis was used to examine differences in demographic and clinical characteristics. To verify the homogeneity between groups, the chi-square test was used for categorical data, whereas the independent t-test was used for continuous data. Inferential statistical analysis consisted of generalized estimating equations (GEE) for repeated-measurement data and one-way analysis of covariance (ANCOVA) for two-endpoint data was used to test the intervention effects. The 5% level of significance was used to confirm.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board of the study hospital (IRB Ref No. 201600926B0) before the study. All participants gave written informed consent after fully explaining the research purpose and process. Participants were informed that they could withdraw from the study at any time, without any negative consequences. Confidentiality of their identities and research data was also ensured.

Results

The results of baseline characteristics of participants

As shown in Figure 1, of the 101 participants who were eligible, 92 signed informed consent, and eventually 86 completed the study. Six participants withdrew from this study due to the lack of interest intension ($n = 3$), the loss of contact ($n = 1$), treatment change ($n = 1$), and disease progress ($n = 1$), with an attrition rate of 6.5%. Table 1 summarizes the demographic and clinical characteristics of the participants. The mean age was 55.86 (SD 9.03) and 53.95 (SD 9.34) years in the AcuCare and control groups, respectively. There were no significant group differences in participants' characteristics, except for the oral mucositis grade ($\chi^2 = 5.72$, $P = 0.03$).

The results of outcomes of pain intensity, negative moods, and quality of life

Figure 3 shows the trends of pain intensity and negative moods overtimes for two groups. All outcomes present the increasing trend, with poor results in the control group compared to AcuCare group. At baseline, there were no significant group differences in the pain intensity and negative moods ($P > 0.05$). Furthermore, Table 2 shows parameter estimates and their standard errors for a model with an autoregressive order 1 autocorrelation and robust-based estimates of the variance in GEE models. After adjusting the oral mucositis grade at each time point, no significant group-difference prevailed in pain intensity ($P > 0.05$). The interactions between time and group cause significant increase in pain intensity for both groups at Weeks 1, 2, 3, and 6 ($P < 0.05$) compared to baseline, indicating time-dependent growth effects. However, the AcuCare group had a lower increase progress ($\beta = 0.77, 1.87, 1.98, 2.88$) than that in the control group ($\beta = 0.92, 2.50, 2.45, 2.99$). In the outcome of negative moods, there was no significant difference between groups and between time and group ($P > 0.05$).

Table 3 shows the results of the ANCOVA for the QoL. At baseline, there were no significant group differences in the seven symptom subscales of QoL ($P > 0.05$). After adjusting the oral mucositis grade at baseline, a significant group-difference was found in the subscale of senses problems at Week 6 ($F = 7.33$, $P = 0.01$). There was no significant group-difference in the remaining subscales of pain, swallowing, speech problems, trouble with social eating, trouble with social contact, and less sexuality ($P > 0.05$).

Table 1
Demographic and clinical characteristics of participants at baseline.

Variable	AcuCare ($n = 44$), n (%)	Control ($n = 42$), n (%)	t/χ^2	P
Age [mean (SD), years]	55.86 (9.03)	53.95 (9.34)	0.82	0.36
Gender			0.80	1.00[a]
Male	39 (88.6)	38 (90.5)		
Female	5 (11.4)	4 (9.5)		
Marital			1.55	0.21
Single	11 (25.0)	6 (14.3)		
Married	33 (75.0)	36 (85.7)		
Education			1.63	0.44
Junior high and below	20 (45.5)	20 (47.6)		
Senior high	21 (47.7)	16 (38.1)		
College and above	3 (6.8)	6 (14.3)		
Smoking history			0.14	0.93
None	9 (20.5)	10 (23.8)		
Quit	13 (29.5)	12 (28.6)		
Yes	22 (50.0)	20 (47.6)		
Drinking history			3.03	0.21
None	18 (40.9)	10 (23.8)		
Quit	12 (27.3)	13 (31.0)		
Yes	14 (31.8)	19 (45.2)		
Betel quid			3.17	0.20
None	20 (45.5)	12 (28.6)		
Quit	16 (36.4)	17 (40.5)		
Yes	8 (18.2)	13 (31.0)		
Tumor site			1.85	0.39
Oral cavity	25 (56.8)	28 (66.7)		
Pharynx	14 (31.8)	8 (19.0)		
Nasopharynx	5 (11.4)	6 (14.3)		
Stage			1.44	0.48
II	8 (18.2)	4 (9.5)		
III	3 (6.8)	4 (9.5)		
IV	33 (75.0)	34 (81.0)		
Surgery			0.37	0.54
None	14 (31.8)	16 (38.1)		
Yes	30 (68.2)	26 (61.9)		
Mucositis				
Grade 0	36 (81.8)	41 (97.6)	5.72	0.03[a]
Grade 1	8 (18.2)	1 (2.4)		
Drug for chemotherapy			0.50	0.48
Platinum	39 (88.6)	35 (83.3)		
Others	5 (11.4)	7 (16.7)		
Radiotherapy total dose (Gy)	6794.09 (498.02)	6895.14 (292.67)	−0.73	0.34

[a] Fisher's exact test

Discussion

The results of this study indicate that acupoint stimulation of combined TAES and AA slightly reduced pain intensity in HNC patients during CCRT. There was an upward trend in pain intensity over time, and the increased progress over time was obviously lower in those of the AcuCare group than the control group at the end of the intervention. In cancer patients,

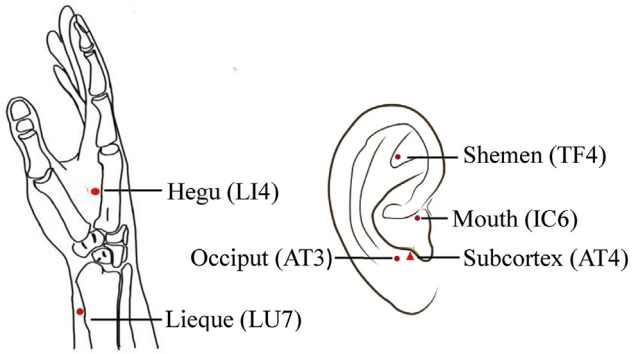

Figure 2. The location of body and auricular acupoints.

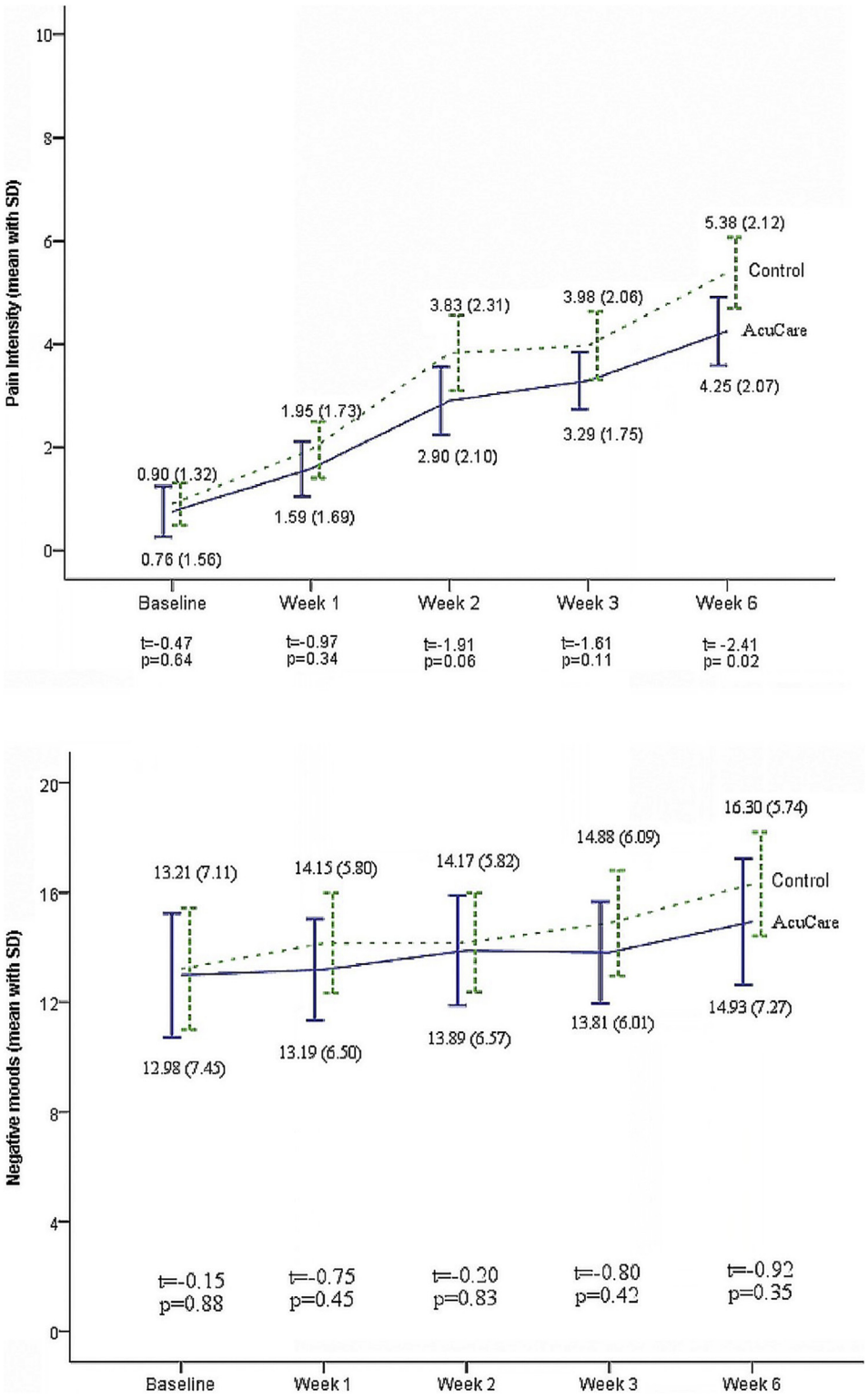

Figure 3. The trend of outcomes on pain intensity and negative moods.

treatment-induced pain gets progressively worse with increasing cumulative radiation doses.[11] In particular, the head and neck area are highly sensitive to pain.[49] One systematic review concluded that acupuncture ineffectively reduced chemotherapy- or radiotherapy-induced pain.[30] In contrast, regarding reducing cancer pain, many studies indicated acupoint stimulation was effective.[25,34,35,39,50] These inconsistencies may be due to stimulation techniques, stimulus dose, and even cancer therapeutic modalities and pain etiology. Stimulating body acupoints to relieve pain is to dredge their corresponding meridians, which improves qi stagnation and blood stasis, and finally restores body function according to the TCM principles.[16,43] In addition, the mechanism for acupoint stimulation alleviates pain is to increase β-endorphin and decrease the substance neurotransmission.[51] In particular, LI4[24] and LU7[52] work effectively on pain reduction through applying TAES. The mechanisms of AA could be also

Table 2
Results of the generalized estimating equations analysis for the outcomes.

Variables	Beta	SE	95% CI	Wald χ^2	*P*
Pain intensity					
Intercept	0.90	0.20	0.50~1.29	19.63	< 0.001
AcuCare†	−0.21	0.32	−0.83~0.41	0.45	0.50
AcuCare × Week 1‡	0.77	0.27	0.24~1.31	8.06	0.01
AcuCare × Week 2‡	1.87	0.38	1.12~2.63	23.87	< 0.001
AcuCare × Week 3‡	1.98	0.42	1.15~2.80	22.17	< 0.001
AcuCare × Week 6‡	2.28	0.60	1.10~3.46	14.44	< 0.001
Control × Week 1§	0.92	0.23	0.47~1.37	15.91	< 0.001
Control × Week 2§	2.50	0.37	1.77~3.23	45.42	< 0.001
Control × Week 3§	2.45	0.34	1.79~3.11	52.96	< 0.001
Control × Week 6§	2.99	0.70	1.62~4.36	18.34	< 0.001
Negative moods					
Intercept	13.22	1.08	11.11~15.34	150.13	< 0.001
AcuCare†	−0.32	1.56	−3.38~2.74	0.04	0.84
AcuCare × Week 1‡	0.10	1.04	−1.94~2.13	0.01	0.93
AcuCare × Week 2‡	0.74	1.31	−1.83~3.32	0.32	0.57
AcuCare × Week 3‡	0.28	1.23	−2.13~2.68	0.05	0.82
AcuCare × Week 6‡	0.80	1.83	−2.79~4.39	0.19	0.66
Control × Week 1§	0.69	0.84	−0.96~2.35	0.67	0.41
Control × Week 2§	0.60	1.09	−1.53~2.72	0.30	0.58
Control × Week 3§	0.86	1.45	−1.98~3.71	0.35	0.55
Control × Week 6§	1.86	2.09	−2.23~5.96	0.80	0.37

Reference: † control group, ‡ AcuCare × baseline, § control × baseline; × interaction; adjusting mucositis over time.

associated with the autonomic nervous systems, the neuroendocrine system, neuroinflammation, and neural reflex.[53] Auricular acupoints on specific locations of the outer ears to relieve body pathology through applying seeds and pressure to them to yield effects of pain reduction.[35–37]

Table 3
Results of the ANCOVA analysis for the quality of life.

Variables	Baseline			Week 6		
	Mean (SD)	*t*[a]	*P*	Mean (SD)	*F*[b]	*P*
Pain						
AcuCare group	7.01 (11.50)	−1.29	0.20	25.91 (20.10)	1.61	0.21
Control group	10.25 (11.82)			33.00 (22.79)		
Swallowing						
AcuCare group	18.37 (21.31)	−1.32	0.19	46.65 (21.89)	0.02	0.90
Control group	24.80 (23.96)			54.17 (18.48)		
Senses						
AcuCare group	10.98 (19.99)	0.25	0.80	48.17 (27.98)	7.33	0.01
Control group	9.92 (19.50)			60.96 (22.52)		
Speech						
AcuCare group	20.45 (27.32)	−0.16	0.87	34.15 (28.59)	0.09	0.77
Control group	21.43 (27.48)			34.21 (21.83)		
Social eating						
AcuCare group	12.73 (15.41)	−1.56	0.12	37.40 (18.51)	1.47	0.23
Control group	27.58 (24.52)			43.09 (17.31)		
Social contact						
AcuCare group	12.73 (15.41)	−0.83	0.41	17.89 (18.27)	1.31	0.26
Control group	15.71 (17.96)			23.33 (14.14)		
Less sexuality						
AcuCare group	28.41 (27.74)	0.10	0.92	33.33 (31.18)	0.38	0.54
Control group	27.78 (30.06)			39.04 (26.64)		

[a] Independent *t*-test.
[b] ANCOVA with mucositis covariate at baseline.

Noted that radiation dermatitis and mucositis were more serious during the CCRT period.[9] In this study, CCRT-induced dermatitis and mucositis could result in hiding the effect of acupoint stimulation for relieving pain in HNC patients. In addition, the radiation dose is associated with otitis media, effusion,[54] tinnitus, and ear obstruction,[55] which affected HNC patients' adherence to press auricular acupoint on the schedule and reduced the required pressing force. This study suggests further research that adopts somatic instead of the auricular acupoint, and increases stimulus dosage corresponding with cumulative treatment for HNC patients receiving CCRT.

In this study, participants who received acupoint stimulation intervention had lower negative moods over time than those did not, although there was no obvious improvement. This finding is similar to a systematic review that the evidence insufficiently supports the effect of acupuncture on relieving depression symptoms for cancer patients.[29] However, the aforementioned studies indicated that it effectively reduced anxiety[24,26,27,38] and depression.[24,28,38] Because these studies specified acupoints for reducing anxiety or depression rather than reducing pain or different target patients. Accordingly, the differences in symptoms and acupoint selected may lead to a different consequence. Additionally, this study found participants' negative moods that continuously increased over a six-week period, especially of who had mild to moderate pain. While the pain could not be relieved sufficiently in this study, the effect of acupoint stimulation may hide its benefit in improving negative moods. To the best of researchers' knowledge, this study is the first of its kind that investigated the effects of acupoint stimulation with TEAS and AA on improving physiopsychological influences from pain and negative moods in HNC patients receiving CCRT. Cancer-related plus CCRT-induced pain is a complex issue, future research simultaneously measuring pain and emotional data to provide empirical evidence is suggested.

This study supports the evidence that acupoint stimulation intervention effectively improved the taste and smell senses difficulty of QoL in HNC patients receiving CCRT. This finding indicated that acupoint stimulation intervention obviously solved taste and smell problem, consistent with previous studies.[25,26,28,29,39] However, two reviews determined insufficient evidence to the effect of acupuncture in improving taste[56] or olfactory dysfunction.[57] Taste and smell changes occurred in HNC patients during the course of the treatment still required attention.[58] Notably, the remaining concerns of QoL had not been improved in this study. As the aforementioned results of pain and negative moods existed, the impact of cancer treatment on QoL was held by the participants. In the future, additional studies are warranted to explore the mechanism of taste and smell disorders from cancer treatment and investigate the benefits of improved taste and smell problems in HNC patients receiving CCRT.

Limitations

This randomized controlled trial has some limitations. Firstly, all participants diagnosed with HNC receiving CCRT were recruited from one hospital, and consequently may not be generalizable to other cancers and different cancer therapies. Second, the participants were concealed to group assignment, but they are aware of their participation in acupoint stimulation intervention or not, possibly inducing performance bias. Third, the researcher nurses who were responsible for implementing the intervention and collecting data were not blinded. Hence, performance bias may not be excluded. Fourth the pain and associated symptoms become progressively worse overtime during the CCRT period, which may require an increase of acupoint stimulation. Lastly, the intervention and measurement were limited to six weeks, and thus a longer-term effect of acupoint stimulation on pain, negative moods, and QoL are unknown.

Conclusions

This study provides the first evidence for the effects of acupoint stimulation on pain relief, negative moods reduction, and QoL in HNC

patients receiving CCRT. This finding indicates that 6-week acupoint stimulation intervention slightly improved pain intensity and effectively improved senses problem of QoL. However, this study did not support the benefit to improve negative moods. Further studies are suggested to conduct a longitudinal research design with extend intervention and follow-up period over six weeks and blinding intervention provider and outcome assessor. With increasing cumulative CCRT treatments, the effects of corresponding increasing stimulus dosage and adopting somatic acupoint is warranted.

Declaration of competing interest

None declared.

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