DOI: 10.31276/VJSTE.2024.0106

Efficacy of auricular acupuncture combined with electroacupuncture for chronic low back pain: A randomised controlled trial

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Received 6 October 2024; revised 25 November 2024; accepted 9 January 2025

Abstract:

Chronic low back pain (CLBP) imposes significant medical treatment costs and leads to numerous serious health consequences. In recent years, non-pharmacological therapies have garnered increasing attention, particularly electroacupuncture (EA) and auricular acupuncture (AA). While considerable research has examined the efficacy of EA and AA in managing CLBP, it may be beneficial to investigate the impact of combining these approaches. This study evaluated the efficacy of a combined AA and EA treatment for CLBP compared to EA alone. This randomised, double-blind, controlled trial allocated 80 patients into two groups: one receiving EA in conjunction with AA at the target points Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4), and the other receiving EA with sham AA (AA applied at non-acupoint locations). Pain intensity, functional disability, and spinal mobility were assessed using the visual analogue scale (VAS), Oswestry disability index (ODI), and Schober index at baseline (T0), after 7 days (T7), and after 14 days (T14). While both groups exhibited improvement, the intervention group demonstrated a greater reduction in VAS scores (T14: 1.65±0.66 vs. 3.28±0.91, p<0.001) and ODI scores (T14: 13.98±1.43 vs. 17.45±1.74, p<0.001), alongside a significant increase in spinal flexibility (Schober index: 14.66±0.80 vs. 13.43±1.04, p<0.001). In conclusion, among patients with CLBP, the combination of AA and EA resulted in more effective pain relief and greater improvement in spinal function compared to EA alone.

Keywords: **auricular acupuncture, chronic low back pain, electroacupuncture.**

Classification numbers: **3.2, 3.6**

1. Introduction

Chronic low back pain (CLBP) is a prevalent musculoskeletal condition that significantly affects individuals' health and quality of life. As a leading cause of disability, CLBP impacts both the physical and psychological well-being of sufferers and imposes a substantial socioeconomic burden globally. Contributing to these challenges, the number of individuals affected by CLBP increased from 377.5 million in 1990 to 577.0 million in 2017, with an age-standardised point prevalence of 7.5% [1, 2].

Pharmacological treatments, particularly nonsteroidal anti-inflammatory drugs (NSAIDs), are commonly used to manage CLBP. However, their long-term use can lead to adverse effects, including gastrointestinal, cardiovascular, and renal complications. Consequently, there has been growing interest in non-pharmacological alternatives for managing CLBP [3].

Recent studies have extensively investigated electroacupuncture (EA), which combines traditional acupuncture with electrical stimulation, to evaluate its efficacy in alleviating pain and improving function in CLBP patients. In addition to EA, auricular acupuncture (AA) has emerged as a promising complementary therapy. AA involves stimulating specific points on the ear that are believed to correspond to different parts of the body [4-6].

Several studies, such as that by A. Ushinohama, et al. (2016) [7], have highlighted that stimulation of auricular

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points, including Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4), can temporarily reduce pain levels in patients suffering from low back pain. This selection of points aligns with traditional medicine theories and is supported by modern research on its analgesic mechanisms. Therefore, we selected this specific AA formula for further analysis [7-12].

This study introduces a novel approach to comparing the effectiveness of two treatment modalities for CLBP. Both groups will receive standard EA treatment, with the intervention group (AA group) receiving additional AA at points associated with pain relief (TF4, AH9, AT4), while the control group (C group) will receive AA at unrelated points. This research aims to determine whether combining AA with EA provides greater pain relief and functional improvement in CLBP patients than standard EA alone.

2. Materials and methods

2.1. Study design

This randomised, double-blind, controlled clinical trial (RCT) was conducted on 80 CLBP patients at the Ho Chi Minh Medical University Hospital, Branch 3, Vietnam, from December 2021 to October 2022. Participants were randomly assigned to either the intervention group (AA group), which received auricular acupuncture combined with electroacupuncture, or the control group (C group), which received sham auricular acupuncture combined with electroacupuncture.

2.2. Sample size

$$n_A = \kappa n_B$$

$$n_B = \left(1+\frac{1}{\kappa}\right)\left(\sigma \frac{z_{1-\alpha/2}+z_{1-\beta}}{A \quad B}\right)^2$$

$$1-\beta = \Phi(z-z_{1-\alpha/2})+\Phi(-z-z_{1-\alpha/2})$$

$$z = \frac{\mu_B-\mu_B}{\sigma\sqrt{\frac{1}{n_A}-\frac{1}{n_B}}}$$

The sample size was determined based on: μA: Visual analogue scale (VAS) of the control group, 3 [13]; μB: VAS of the intervention group, 2 (expected score); Type 1 error: alpha (α)=0.05; Type 2 error: beta (β)=0.2; Standard deviation (σ)=1.5; Sample ratio $\kappa=n_A/n_B$ (control group/ intervention group)=1 [14]; Φ: Normal distribution function $(z_{1-\alpha/2} + z_{1-\beta})^2 = C(\alpha,\beta)=7.9$.

Based on these calculations, each group required a minimum of 36 participants. Considering an estimated dropout rate of approximately 10%, the final sample size for each group was adjusted to 40 participants, resulting in a total study sample of 80 participants.

2.3. Participants

The initial examinations were conducted by a traditional medicine doctor certified by the Practice Certificate, in accordance with the regulations of the Vietnamese Ministry of Health.

Participants were eligible for the study if they:

• Were 18 years of age or older;

• Had CLBP, defined as low back pain persisting for at least three months;

• Were willing to commit to weekly study sessions;

• Reported an average pain intensity score of ≥4 on a 0-10 numerical pain scale in the past week, specifically related to their CLBP [15].

Participants were excluded if they:

• Had a malignant or autoimmune disease, or had experienced recent trauma as the cause of their pain;

• Had an allergy to tape;

• Were experiencing acute back pain [15].

Participants were withdrawn from the study if they:

• Withdrew consent to continue participation;

• Discontinued electroacupuncture treatment for more than three sessions per week;

• Reported a worsening of pain symptoms beyond tolerable levels.

2.4. Blinding

After meeting the inclusion and exclusion criteria, participants were randomly assigned to groups by ballot-blue (AA group) or white (C group). Each participant

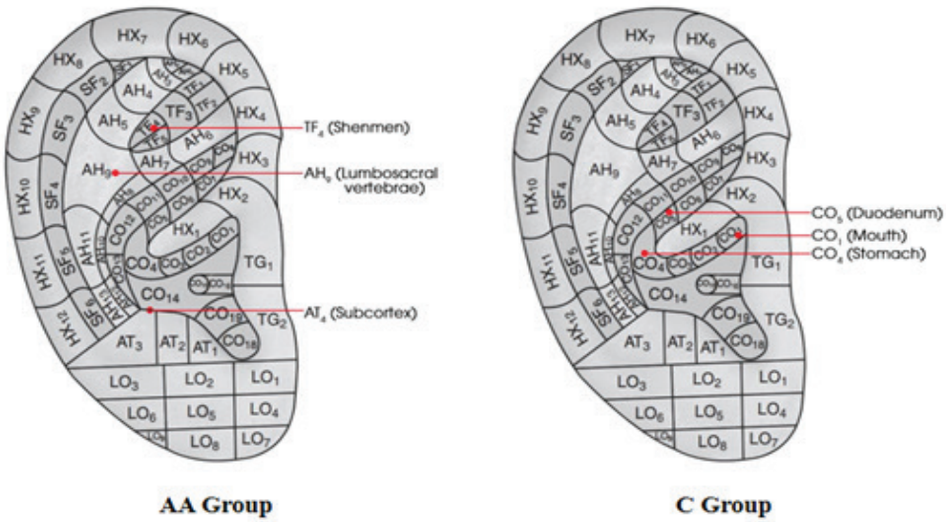

Fig. 1. Location of acupoints utilised in this study, following the Chinese system.

received treatment based on the colour of the ballot after completing assessments in a separate room.

2.5. Study interventions

All participants received treatment from a certified acupuncturist with five years of clinical experience.

Control group (C group): 40 participants were treated with electroacupuncture and auricular acupuncture on sham acupoints in the stomach (CO4), duodenum (CO5), and mouth (CO1) [15].

Intervention group (AA group): 40 participants received electroacupuncture and auricular acupuncture targeting the true tympanic membrane at the Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4) acupoints (Fig. 1) [15].

2.5.1. Electroacupuncture (EA)

The electroacupuncture protocol included four Ashi points (two per side), each corresponding to a specific pain location. The selected Ashi points were Shenshu (BL-23) and Yanglingquan (GB-34), with a stimulation frequency of 60 Hz and a duration of 20 minutes per session. Patients received treatment daily for 14 days, excluding Sundays [16].

2.5.2. Auricular acupuncture (AA)

To alleviate stress and pain, this study employed three auricular acupoints: Shenmen (TF4) (master point for sedation), Lumbosacral Vertebrae (AH9), and Subcortex (AT4), as classified by the World Health Organisation (WHO) for ear acupoint terminology and location.

Procedure: Patients were seated and allowed to rest for 10 minutes before treatment. The therapist disinfected the participant's skin with 70% ethyl alcohol. The study utilised sterile, stainless steel, single-use acupuncture press needles (length: 1.3 mm, diameter: 0.22 mm; Suzhou Hualun Medical Appliance Co., Suzhou, China). Three needles were inserted percutaneously to a depth of 1.3 mm, secured with flesh-coloured adhesive tape, retained in situ, and continuously pressed for three minutes.

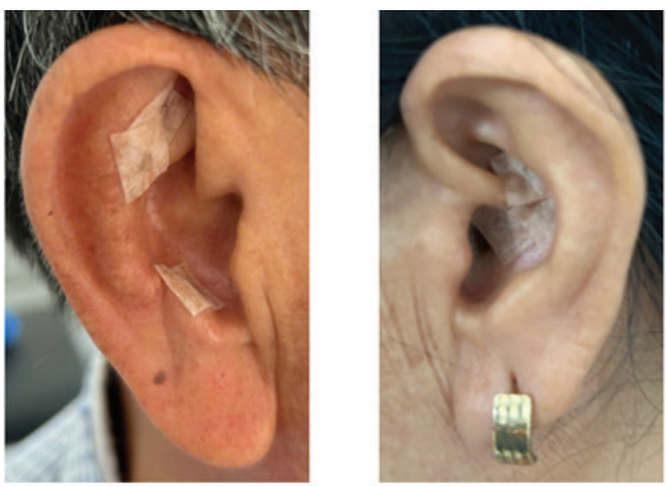

Fig. 2. Depiction of auricular acupuncture points based on the Chinese system.

For the control group, auricular acupuncture was performed at sham acupoints not associated with CLBP, specifically the stomach (CO4), duodenum (CO5), and mouth (CO1) acupoints. The follow-up period required retention of these patches on acupoints for five days per week. Participants were instructed to perform self-acupressure three times daily, pressing each acupoint for 30 seconds per session over a duration of three minutes at home (Fig. 2) [12].

2.6. Outcomes measures

Patient characteristics: Data collected included age, gender, body mass index (BMI), occupation, duration of illness, accompanying diseases, and X-ray findings. Occupations were categorised as follows:

• Light labour: Office work, sedentary or standing for prolonged periods, fixed tasks, no heavy lifting.

• Moderate labour: Jobs involving frequent movement, such as trading, housework, engineering, and carrying loads under 12 kg.

• Heavy labour: Occupations requiring significant physical exertion, including caretakers, construction workers, bike security guards, porters, and agricultural workers, involving loads exceeding 12 kg.

A primary practitioner assessed and measured clinical outcomes at three time points: T0 (baseline), T7 (after seven days), and T14 (after 14 days), using the visual analogue scale (VAS), Oswestry disability index (ODI), and Schober index. Prior to the study, the assessor completed a three-week training programme to ensure standardised evaluation and application of these measurement tools.

• Pain relief: Patients self-assessed their pain level by marking a scale corresponding to their perceived pain intensity [14].

• Oswestry disability index (ODI): This tool measures functional ability in daily activities for individuals with CLBP. It comprises 10 questions, with responses provided on a 6-point Likert scale. Scores range from 0 (no disability) to 100% (severe disability) [17].

• Schober index: This measure evaluates lumbar spine extension during bending movements. A positive Schober's test is defined as a forward flexion increase of less than 5 cm [18].

2.7. Statistical analysis

Data were analysed using STATA version 14. Continuous variables were expressed as mean±standard deviation (SD) and compared using the independent t-test or the Wilcoxon rank-sum test, as appropriate. Categorical variables were reported as frequencies and percentages and compared using the chi-square test or Fisher's exact test when expected frequencies were small. A p-value of <0.05 was considered statistically significant. Intention-to-treat analyses were conducted to account for any potential loss to follow-up.

2.8. Medical ethics

The study received ethical approval from the Medical Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City, under reference No. 1999/QD-DHYD, signed on 6 October 2021.

3. Results

3.1. Patient characteristics

A total of 80 patients who met the inclusion criteria and had no exclusion criteria were randomly assigned to either the C group (n=40) or the AA group (n=40). No patients were lost to follow-up (Fig. 3).

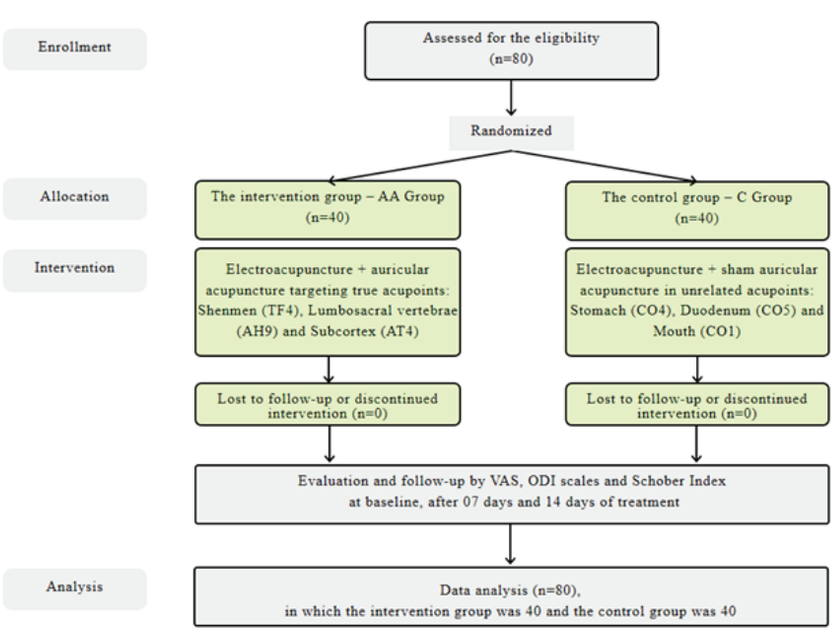

Fig. 3. Flow chart of the study.

Table 1. Initial characteristics of the pre-intervention sample.

Characteristics	C group (n=40)	AA group (n=40)	p-value
Sex (n, %)			
Male	12 (30.0)	12 (30.0)	1[a]
Female	28 (70.0)	28 (70.0)	
Age (year)	60.58±10.96	59.85±8.54	0.427[b]
BMI (n, %)			
Normal	19 (47.5)	21 (52.5)	0.655[a]
Overweight	21 (52.5)	19 (47.5)	
Profession (n, %)			
Light labour	14 (35.0)	15 (37.5)	
Medium labour	12 (30.0)	12 (30.0)	0.965[a]
Heavy labour	14 (35.0)	13 (32.5)	
Disease duration (months, mean ± SD)	29.53±17.13	28.95±16.12	0.881[b]
Comorbidities (n, %)			
High blood pressure	14 (35.0)	20 (50.0)	0.175[a]
Myocardial ischemia	23 (57.5)	25 (62.5)	0.648[a]
Knee osteoarthritis	28 (70.0)	27 (67.5)	0.809[a]
Diabetes	23 (52.5)	24 (60.0)	0.82[a]
Gastritis	21 (52.5)	20 (50.0)	0.823[a]
GERD	16 (40.0)	20 (50.0)	0.782[a]

Note: Qualitative data are presented as frequencies (percentages), while quantitative data are presented as mean ± SD. Abbreviations: SD: standard deviation, BMI: body mass index, GERD: gastroesophageal reflux disease. [a]: Chi-square test; [b]: Wilcoxon signed the rank-sum test.

Table 1 presents the baseline characteristics of the study population.

Demographics: The gender distribution was similar between groups, with 30% male and 70% female participants, showing no statistically significant difference (p=1.000). This ensures that gender-related bias did not influence treatment outcomes. The mean age was comparable between the C group (60.58±10.96 years) and the AA group (59.85±8.54 years, p=0.427), indicating no significant age difference. This age range represents a population commonly affected by chronic conditions, which could impact intervention efficacy.

Body mass index (BMI): There was no notable difference between groups in BMI category distribution (normal vs. overweight, p=0.655). Since BMI is known to contribute to systemic inflammation and potentially influence treatment response, this balance ensures comparability.

Profession: Both groups had a similar distribution of occupational categories (light, medium, and heavy labour; p=0.986), indicating that occupational differences were not a confounding factor.

Disease duration: The mean disease duration was 29.53±17.13 months in the C group and 28.95±16.12 months in the AA group (p=0.881), demonstrating that participants in both groups were at comparable stages of disease progression.

Comorbidities: There were no significant differences between groups regarding the prevalence of comorbid conditions, including hypertension, myocardial ischaemia, knee osteoarthritis, diabetes, gastritis, and gastro-oesophageal reflux disease (GERD). This indicates that comorbidities were well balanced across the study population.

3.2. Outcomes

Table 2. Pain relief in control (C) group and auricular acupuncture (AA) group.

Timepoint	C group (n=40)	AA group (n=40)	p-value
T0 (Baseline)	6.23±0.44	6.33±0.62	0.669[b]
T7	4.73±0.82	3.95±0.93	<0.001[b]
T14	3.28±0.91	1.65±0.66	<0.001[b]
T14-T0	-2.95±0.56	-4.68±0.72	
p-value (T14-T0)	<0.001[b]	<0.001[b]	

Note: Values are presented as mean ± SD. Abbreviations: VAS (visual analogue scale). The statistically significant difference with p<0.05. [b]: Wilcoxon signed rank-sum test.

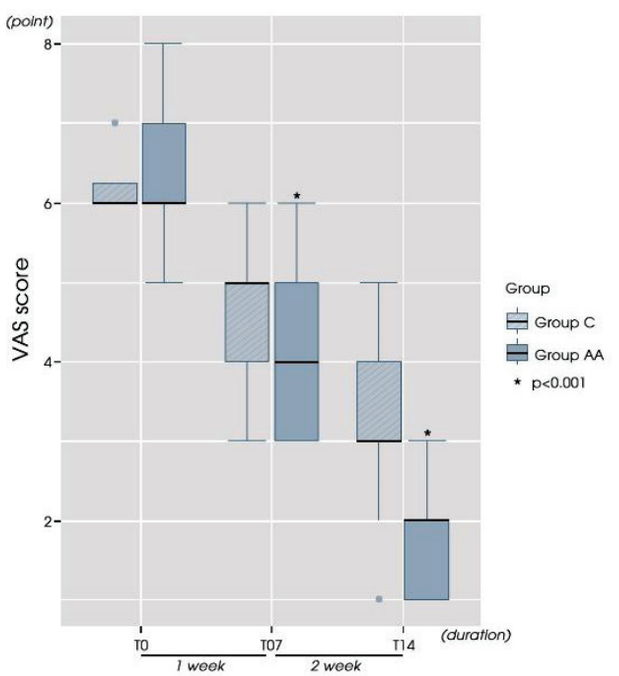

Fig. 4. Visual analogue scale improvement over time for the two groups.

Table 2 illustrates the effects of treatment over time. A comparison of pre- and post-treatment data reveals that VAS scores in both the C group and AA group decreased significantly after 14 days of treatment, demonstrating the clinical effectiveness of electroacupuncture and auricular acupuncture (AA) combined.

At baseline (T0), the mean VAS scores between the C group and AA group were similar, with no statistically significant difference. By day 7 (T7), both groups experienced significant reductions in pain, with the AA group exhibiting a greater decrease than the C group, indicating a more pronounced and earlier pain relief effect in the intervention group. By day 14 (T14), the AA group continued to show greater pain relief than the C group, a trend that persisted, demonstrating the sustained efficacy of the AA intervention (Table 2 and Fig. 4 depict VAS improvement over time for both groups). Notably, participants in the AA group experienced nearly twice the pain reduction compared to those in the C group, a difference that was statistically significant. These findings suggest that the intervention in the AA group provided more effective and faster pain relief than electroacupuncture alone.

Table 3. Oswestry disability index (ODI) in control (C) group and auricular acupuncture (AA) group.

Timepoint	C group (n=40)	AA group (n=40)	p-value
T0 (Baseline)	39.73±3.27	40.05±3.15	0.622 [b]
T7	27.28±1.71	22.93±2.58	<0.001 [b]
T14	17.45±1.74	13.98±1.43	<0.001 [b]
T14 - T0	-22.28±2.24	-26.07±2.35	
p-value (T14-T0)	0.033[b]	<0.001[b]	

Note: Values are presented as mean ± standard deviation. ODI (Oswestry disability index). The statistically significant difference with p <0.05. [b]: Wilcoxon signed the rank-sum test.

Table 3 presents changes in Oswestry disability index (ODI) scores, highlighting improvements in functional ability. A comparison of pre- and post-treatment scores within each group indicates significant improvements in ODI scores in both groups. At baseline (T0), the mean ODI scores were comparable between the C group and AA group, with no statistically significant difference, confirming the homogeneity of disability levels before the intervention. By day 7 (T7), both groups demonstrated substantial improvements in disability, with the AA group exhibiting a greater reduction in ODI scores than the C group, suggesting earlier improvements in lumbar spine function. By day 14 (T14), this difference remained consistent, with the AA group continuing to exhibit lower ODI scores than the C group, reinforcing the sustained superiority of the AA intervention

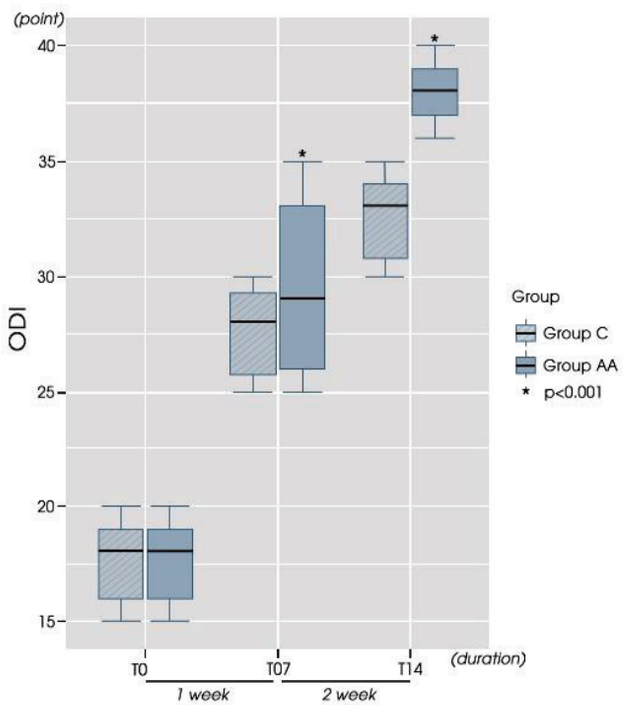

Fig. 5. Lumbar spine function improvement according to Oswestry disability index (ODI) over time.

(Table 3 and Fig. 5 illustrate ODI score improvements over time for both groups). These reductions exceeded the minimal clinically important difference (MCID) threshold of 12 points, indicating that the observed improvements in functional outcomes were not only statistically significant but also clinically meaningful, particularly in the AA group.

Table 4. Schober index (Spinal flexibility) in control (C) group and auricular acupuncture (AA) group.

Timepoint	C group (n=40)	AA group (n=40)	p-value
T0 (Baseline)	12.70±1.86	12.30±1.57	0.301 [b]
T7	13.28±1.54	13.70±1.16	0.254 [b]
T14	13.43±1.04	14.66±0.80	<0.001[b]
T14-T0	0.73±1.72	2.36±1.34	
p-value T0 with T14	0.033[b]	<0.001[b]	

Note: Values are presented as mean ± standard deviation. The statistically significant difference with p<0.05. [b]: Wilcoxon signed the rank-sum test.

Table 4 presents schober index improvements across both groups following treatment. When comparing pre- and post-treatment results within each group, the AA group demonstrated a greater increase in Schober index values

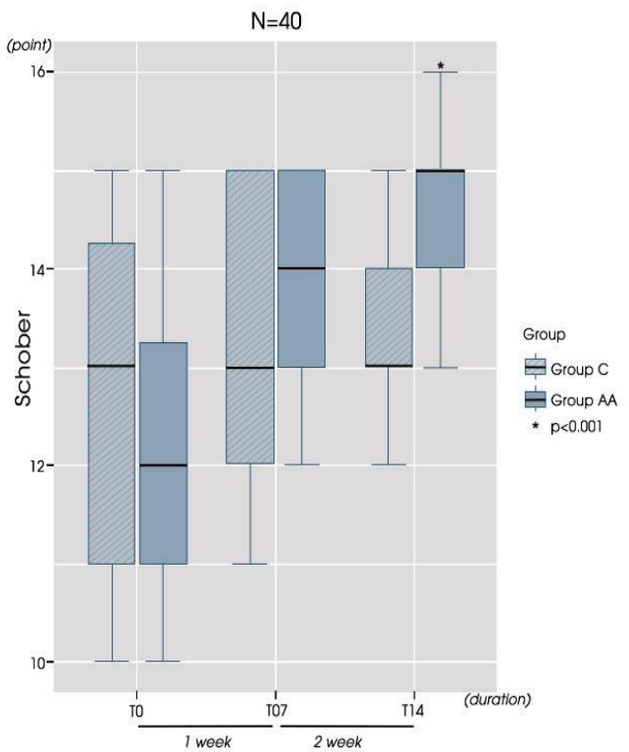

Fig. 6. Schober amplitude improvement over time.

than the C group, indicating the enhanced efficacy of electroacupuncture combined with auricular acupuncture. At baseline (T0), the mean schober index was similar in both groups, with no statistically significant difference. By day 7 (T7), the AA group exhibited slightly greater spinal flexibility than the C group, although this difference was not statistically significant. By day 14 (T14), the AA group displayed a significantly greater reduction in spinal inflexibility, far exceeding that observed in the C group (Table 4 and Fig. 6 illustrate Schober index improvements over time for both groups). The AA group's improvements in Schober index scores indicate meaningful enhancements in spinal mobility, which were both statistically significant and clinically relevant.

These findings consistently demonstrate that auricular acupuncture significantly enhances pain relief, reduces disability, and improves physical function, as evidenced by improvements in VAS, ODI, and Schober index scores.

4. Discussion

4.1. General characteristics of the study sample

The patient sample in this study exhibited a consistent distribution of sex, age, BMI, profession, and comorbidities between the AA group and the control group (C group), minimising potential confounding factors. This homogeneity ensured an accurate comparison of treatment effects between the groups. The similar distribution of occupational categories and BMI reduced the likelihood of biased outcomes, consistent with previous studies on chronic lumbar spine conditions in older populations [19].

4.2. The pain-relieving effectiveness of combining electroacupuncture and auricular acupuncture

Electroacupuncture (EA) is an acupuncture technique that combines electrical stimulation with acupuncture needles to enhance its pain-relieving effects. Numerous recent studies have demonstrated the effectiveness of EA in treating back pain and other conditions. Several physiological mechanisms explain the analgesic effects of electroacupuncture:

(1) When acupuncture needles are driven with electrical current, they activate nerve fibres-especially Aδ and C fibres-which in turn stimulate the spinal cord and brain to produce neurotransmitters such as endorphins, enkephalins, serotonin, and dynorphins, facilitating natural pain relief.

(2) Electroacupuncture promotes the release of endogenous opioids, gamma-aminobutyric acid (GABA), and serotonin, which activate the descending pain inhibition pathways in the brain and block pain signals at the dorsal horn of the spinal cord.

(3) Electroacupuncture modulates the "pain gate" mechanism in the spinal cord, reducing pain signal transmission from peripheral nerves to the brain and thereby lowering pain perception.

(4) The microcurrents generated by acupuncture needles improve blood circulation in the affected area, reducing inflammation and oedema, which further alleviates pain.

(5) Electroacupuncture has been shown to effectively alleviate symptoms of chronic pain [20-22].

Auricular acupuncture (AA) is widely used in the treatment of CLBP. In this study, acupoint selection was based on the anatomical relationship between the auricular surface and the lower back. The study utilised the WHO's classification of auricular acupoints, which are believed to influence the meridians and blood circulation, thereby alleviating pain symptoms. Traditional Chinese medicine suggests that the ear is connected to numerous nerves that regulate the brain, spinal cord, and sympathetic nervous system [19].

In the intervention group (AA group), patients received auricular acupuncture at Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4) - acupoints that correspond to lumbar dysfunction and are commonly used in pain management. The pain-alleviating effects of this combination can be explained through the following mechanisms:

(1) These acupoints regulate central nervous system activity, thereby reducing pain signal transmission to the brain.

(2) Stimulation of these sites promotes the release of endorphins, serotonin, and dopamine, which are natural analgesic compounds.

(3) Auricular acupuncture helps maintain balance between the sympathetic and parasympathetic nervous systems, reducing stress and anxiety-related pain [21, 23, 24].

Additionally, previous studies have demonstrated that auricular acupuncture at Shenmen, the sympathetic point, and nervous subcortex points can reduce back pain, decrease inflammatory markers (IL-1β, IL-2, IL-6), and increase anti-inflammatory cytokines (IL-4) [13, 14, 17]. In contrast, participants in the C group received auricular acupuncture at the following pseudo-atrium acupoints: stomach (CO4), duodenum (CO5), and mouth (CO1) [15], which were selected due to their distant anatomical location from the lumbar region and lack of therapeutic effects on back pain [25, 26]. Furthermore, using equivalent control points helped improve blinding and research objectivity.

This study employed a combined approach to enhance pain management in chronic low back pain patients. The results demonstrated statistically significant improvements in VAS, ODI, and Schober Index scores within each group after 14 days of treatment, confirming the therapeutic effectiveness of both electroacupuncture alone and electroacupuncture combined with auricular acupuncture (AA).

When comparing intervention outcomes between groups, the AA group exhibited greater pain relief than the C group, as reflected in the VAS and ODI scores by day 7. Notably, only the AA group showed significant improvements in the Schober Index by day 14, reinforcing the effectiveness of combining electroacupuncture and AA. These findings align with previous research by L.T.H. Nhung (2019) [19].

The results of this study are consistent with findings from Y.J. Cho, et al. (2013) [27], which demonstrated that acupuncture significantly reduced VAS and ODI scores compared to sham acupuncture over six weeks. In addition, auricular acupuncture for seven weeks was equally effective as standard acupuncture and provided long-term pain relief. Notably, the study highlighted that hand-ear acupuncture yielded superior results compared to conventional acupuncture.

In contrast, the present study combined EA and AA for 14 days and found that pain relief began as early as day 7 and persisted until day 14. Compared to previous studies, the analgesic effects occurred more quickly, and the treatment duration was shorter. Furthermore, this study emphasises the pain-relieving effects of auricular acupuncture at Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4), supporting findings from A. Ushinohama, et al. (2016) [7]; Y.J. Cho, et al. (2013) [27]; and Y. Luo, et al. (2019) [28].

This was a randomised, controlled, double-blind clinical experiment evaluating the effects of auricular acupuncture combined with electroacupuncture on VAS pain intensity, ODI scores, and Schober index improvement in chronic low back pain patients. The findings suggest that the two approaches demonstrate a trend toward faster and more efficient pain reduction than applying one technique alone.

4.3. Limitations

A key limitation of this study was the short 14-day follow-up period, which did not allow for an assessment of the long-term efficacy of the interventions, particularly after treatment cessation. Future studies should incorporate extended follow-up periods to evaluate symptom recurrence and the sustainability of treatment outcomes beyond the intervention period.

5. Conclusions

In conclusion, combining electroacupuncture with auricular acupuncture at Shenmen (TF4), Lumbosacral Vertebrae (AH9), and Subcortex (AT4) effectively reduces VAS and ODI scores after 7 days and improves the Schober index after 14 days of treatment. However, this study primarily demonstrated short-term pain relief and improvements in lumbar spine function. The long-term efficacy of this combined approach remains uncertain and requires further investigation to assess pain recurrence rates following treatment.

CRediT author statement

Diem Huong Thi Nguyen: Conceptualisation, Methodology, Validation, Formal analysis, Data curation, Visualisation, Supervision, Writing - Reviewing; Son Thi Nguyen: Conceptualisation, Methodology, Validation, Formal analysis, Visualisation, Supervision; Minh Quan Hoang Le: Validation, Formal analysis, Data curation, Methodology, Writing - Reviewing, and Editing; Ngoc Nghia Thi Nguyen: Formal analysis, Writing - Reviewing, and Editing; Thuong Hoai Nguyen: Writing - Reviewing, and Editing; Bao Ngoc Le: Formal analysis, Writing - Reviewing, and Editing; Thuc Anh Ho: Writing - Reviewing, and Editing.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

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