INTRODUCTION

Review question / Objective: Some study suggested that electro-acupuncture is effective and safe for chronic pain. But it is controversial.

Condition being studied: Numerous studies have shown that electro-acupuncture is effective in relieving pain. However, the efficacy of electroacupuncture in the treatment of pain remains controversial. With the increase in the number of randomized controlled clinical studies, a meta-analysis for conducting electroacupuncture for chronic pain relief is available.

METHODS

Participant or population: All subjects (18 years and above) who meet one of the
following diagnostic criteria for chronic pain irrespective of gender, race, or nationality.

**Intervention:** The experimental group consisted of patients that received electro-acupuncture or electro-acupuncture plus antidepressants. The acupoint numbers, retaining time and frequency, treatment sessions were not limited.

**Comparator:** The experimental group consisted of patients that received electro-acupuncture or electro-acupuncture plus antidepressants. The acupoint numbers, retaining time and frequency, treatment sessions were not limited.

**Study designs to be included:** The experimental group consisted of patients that received electro-acupuncture or electro-acupuncture plus antidepressants. The acupoint numbers, retaining time and frequency, treatment sessions were not limited.

**Eligibility criteria:** Patients: We defined the Chronic musculoskeletal pain as a current episode lasting at least four weeks (considering that many studies defined the criteria for Chronic musculoskeletal pain as pain lasting for four weeks, for the sake of more possible studies to be included, we also defined Chronic musculoskeletal pain as pain lasting more than four weeks and also performed subgroup analyses for the included subjects with pain duration greater than three months and less than three months in the outcome analysis), including osteoarthritis, non-specific shoulder and low back pain, non-specific back, neck pain, limb pain, cervical pain, thoracic pain, or spondylosis. The pain associated with specific pathologies (e.g., fracture, tumor, etc.) will be excluded. All patients, regardless of gender, race, color, or region, are at least 18 years old.

**Quality assessment / Risk of bias analysis:** The risk of bias of eligible trials was measured by the Risk of Bias (ROB) Tool in Cochrane Handbook (5.1.0) by two independent researchers. Each criterion was graded as "low" risk of bias, "high" risk of bias and "unclear" risk of bias. The methodology quality was assessed by two
independent investigators with the Jadad scale. Any dissent occurred in the assessment procedures was judged by a third investigator.

**Strategy of data synthesis:** Paired meta-analysis, and cumulative meta-analysis were conducted by with random effects model in STATA 15.0 software. Standard mean differences (SMD) with 95% confidence interval (CI) were calculated for HAMD score and changes in HAMD, and risk ratio (RR) with 95% CI for adverse effect. $I^2$ was used to evaluate heterogeneity. Sensitivity analysis and meta-regression analysis were conducted to explore the source of heterogeneity for $I^2>50\%$. Funnel plot was used for digital-based modelling of results. Egger's test was performed to explore potential publication biases. TSA 0.9.5.10 β software (Copenhagen Trial Unit, Copenhagen, Denmark) was used to perform TSA for required information size (RIS) estimate with 0.05 for type I error ($\alpha$) and 0.2 for type II errors (β). Biggerstaff and Tweedie (BT) random effects model was used to explore uncertainty of variance estimation between model tests of random effects. Clinical trials with large sample sizes were given more weight and used for TSA. Invalid boundary was formed by β consumption function reported by O’Brien-Fleming. Sequential monitoring boundaries were formed by α consumption function described by O’Brien-Fleming. Z-curve was generated using cumulative Z-value(40), and RIS was calculated by sample size estimation.

**Subgroup analysis:** We plan to explore reasons for heterogeneity between studies, and check the results through sensitivity analyses. If sufficient trials are included, we will explore the following potential sources of heterogeneity using subgroup analyses or meta-regression:
1. Studies with low risk of bias compared to trials with high risk of bias;
2. Frequency or intensity of intervention;
3. Different disease types; etc.

**Sensitivity analysis:** Sensitivity analysis will be performed to assess the stability of the findings.

**Country(ies) involved:** China.

**Keywords:** Electro-Acupuncture; Chronic musculoskeletal pain; Meta-Analysis; Trial Sequential Analysis.

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