Electroacupuncture for Painful Diabetic Peripheral Neuropathy: A Multicenter, Randomized, Assessor-Blinded, Controlled Trial

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Diabetes Care 2018;41:e141–e142 | https://doi.org/10.2337/dc18-1254

Painful diabetic peripheral neuropathy (PDN) is one of the most common complications of diabetes. In patients with PDN, greater pain intensity leads to poorer quality of life, sleep, function, and work productivity (1–3). According to the clinical practice guideline, electrical stimulation is probably effective and should be considered for the treatment of PDN (evidence level B) (4). The aim of this study is to evaluate the effectiveness and safety of electroacupuncture (EA) for the management of PDN in patients with type 2 diabetes.

This multicenter, randomized, assessor-blinded, controlled trial was conducted between June 2014 and March 2016 at four centers in South Korea (clinical trial reg. no. KCT0001135, https://cris.nih.go.kr). A total of 126 participants with a ≥6-month history of PDN and a mean weekly pain score of ≥4 on the Pain Intensity Numerical Rating Scale (PI-NRS) were randomly assigned in a 1:1 ratio to an EA group ($n = 63$) or control group ($n = 63$). Randomization was performed by using a computer-generated random code, and allocation concealment was achieved using sequentially numbered, opaque sealed envelopes. The participants in the EA group received EA treatment with a mixed current of 2 Hz/120 Hz at 12 acupuncture points (bilateral Zusanli [ST36], Xuanzhong [GB39], Yinlingquan [SP9], Sanyinjiao [SP6], Taichong [LR3], and Zulinqi [GB41]) twice per week for 8 weeks. Depending on the sites of pain, the additional acupuncture point Bafeng (EX-LE10) was available. The locations of acupuncture points were determined according to the general guidelines published by the World Health Organization (5). Participants in the control group did not receive any EA treatment. Education on diet and lifestyle modification for diabetes was provided to both groups through a brochure. Antidiabetes medications were allowed with stable doses throughout the study. The participants in both groups were allowed to take a rescue medication (acetaminophen 500 mg, with a maximum dosage of 3,000 mg per day), but no other analgesic medication was permitted during the study. The intent-to-treat analysis was used in the main analysis. Missing data were imputed by multiple imputations. To compare the groups, a *t* test was used for continuous data, and the categorical data were analyzed with a χ^2 test or Fisher exact test.

Of the 126 patients, 106 (84.1%) completed the 8-week treatment and 98 (77.8%) completed the 8-week follow-up assessment. Nine participants in the EA group and 19 in the control group dropped out during the study. There were no significant differences between groups in any of the demographic characteristics, including age, sex, duration of diabetes (EA group 12.53 years, control group 11.32 years), pain duration (EA group 3.81 years, control group 3.23 years), and antidiabetes medication use. The primary outcomes were PI-NRS score and the proportion of responders (defined as achieving a reduction of ≥50% on the PI-NRS) at the 9th week. For the PI-NRS scores, patients in the EA group showed significantly more improvement than those in the control group (least squares mean difference −0.67 [95% CI −1.29 to −0.06]; $P = 0.0136$) (Fig. 1*A*). Among the patients receiving EA treatment, nine (15.52%) were responders, while only three (6.25%) patients in the control group were responders ($P = 0.2176$) (Fig. 1*B*). The EA treatment group also showed significantly greater improvement than the control group on the short-form McGill Pain Questionnaire, sleep

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Received 10 June 2018 and accepted 5 July 2018.

Clinical trial reg. no. KCT0001135, https://cris.nih.go.kr.

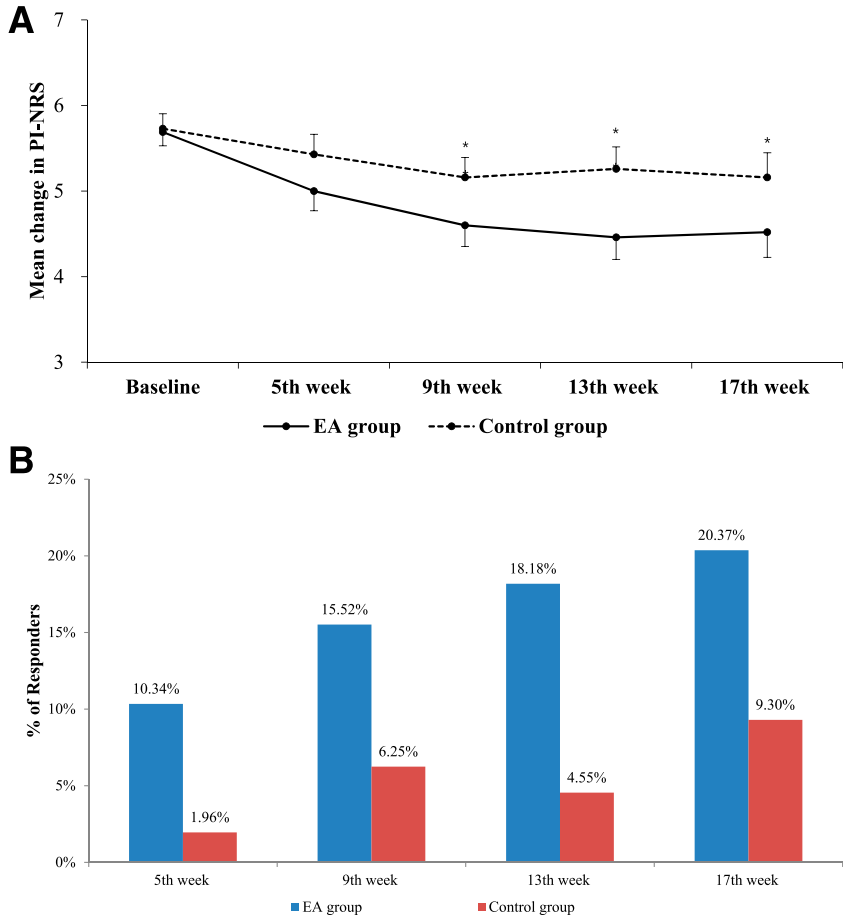

Figure 1—Weekly mean changes from baseline in PI-NRS score (*A*) and the proportion of responders, defined as those achieving a ≥50% reduction in PI-NRS score from the baseline score (*B*). *$P < 0.05$.

interference scores, and the EuroQol-5 Dimensions questionnaire at the 9th week ($P < 0.05$). The percentage of patients reporting improvement in the Patient Global Impression of Change was greater in the EA group (82.5%) than in the control group (34.1%) at the 9th week. This improvement was maintained throughout the study. However, there were no differences in rescue medication consumption or nerve conduction studies between groups. With respect to the safety of EA, there was no significant difference in the incidence of adverse events (AEs) and serious adverse events (SAEs) between groups (EA group: 12 AEs and 3 SAEs; control group: 12 AEs and 3 SAEs; $P = 0.9999$). None of the AEs that occurred were related to EA treatments, and laboratory evaluations were unremarkable.

To our knowledge, this is the first multicenter randomized controlled trial to evaluate the effectiveness and safety of EA treatment for the management in PDN. One limitation is that neither a placebo nor sham EA was used as an active control; therefore, the possibility of a placebo effect was not excluded.

In conclusion, the results of this study demonstrate that EA treatment is effective for reducing pain and improving sleep disturbance and quality of life in PDN. In addition, EA treatment was well tolerated and safe during this study. These findings suggest that EA treatment may be recommended as a nonpharmacological treatment for pain reduction in PDN.

Acknowledgments. The authors would like to express their appreciation for the valuable contributions of the participants with PDN in this trial.

Funding. This work was supported by the Korea Institute of Oriental Medicine grant K14011.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. K.-M.S. contributed to the design of the study and drafted the manuscript. S.L., E.Y.L., C.-H.K., J.W.K., and C.K.L. participated in the design of the study and contributed to a critical review of the manuscript. B.-N.S., A.-R.K., and S.-Y.J. participated in the coordination of the study, and O.K. was involved in the statistical analysis. S.-M.C. supervised the overall design of the study as the principal investigator. All authors read, revised, and approved the final manuscript in its current form. S.-M.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. The protocol of this study was presented as a poster at the 9th Congress of the European Pain Federation, Vienna, Austria, 2–5 September 2015.

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