Effect of neuromuscular electrical stimulation for endometriosis-associated pain

A retrospective study

Xue-ling Bi, MBa, Cai-xia Xie, MBb,∗

Abstract
This retrospective study evaluated the effect of neuromuscular electrical stimulation (NMES) for the treatment of endometriosis-associated pain (EAP). A total of 154 patients with EAP were included and were divided into 2 groups in this retrospective study. Eighty-three patients were assigned a treatment group, and underwent NMES therapy, while 71 subjects in the control group were at waiting list. The primary outcome of pain was measured by the numerical rating scale (NRS) and the Endometriosis Symptom Severity scale (ESSS). The secondary outcome was quality of life, measured by the 36-Item Short Form Health Survey (SF-36). All outcomes were measured before and after 5-week and 10-week treatment. Moreover, we also recorded the adverse events in this study.

After 5-week treatment, no significant differences in all outcome measurements were found between the 2 groups. However, after 10-week treatment, NMES therapy exerted better outcomes in NRS (P<.02), ESSS (P<.04), and SF-36 [Physical Component Summary (PCS), P<.01; Mental Component Summary (MCS), P<.01], compared with the patients at the waiting list. Moreover, no significant differences of all adverse events were found between the 2 groups, although mild and acceptable adverse events occurred in the treatment group.

This study demonstrated that NMES is effective for treating patients with EAP.

Abbreviations: CV 3 = Zhongji, CV 4 = Guanyuan, EAP = endometriosis-associated pain, ESSS = Endometriosis Symptom Severity score, MCS = Mental Component summary, NMES = neuromuscular electrical stimulation, NRS = numerical rating scale, PCS = Physical Component Summary, SF-36 = 36-Item Short Form Health Survey, SP 6 = Sanyinjiao.

Keywords: effect, endometriosis-associated pain, neuromuscular electrical stimulation

1. Introduction
Endometriosis is a very common condition for women at reproductive age.[1–3] It has been reported that about 6% to 10% women experience such condition.[4,5] It mainly manifests as the dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia, especially as the endometriosis-associated pain (EAP).[6–9] It can result in frequent chronic pain and even infertility, if such condition cannot be treated very well.[10–13] Many factors may lead to this issue, including retrograde menstruation, genetic, environment, and immune factors.[14,15] Several treatment strategies are utilized to treat such condition, including oral contraceptives,[16,17] progestin monotherapy,[18,19] danazol,[20] and gonadotropin-releasing hormone.[21] However, all those therapies are still inadequate, and often result in lots of adverse events. Thus, efficacious and safe treatments for long-term intervention for such condition are still needed.

It has been reported that complementary and alternative medicine can treat EAP, such as Chinese acupuncture, moxibustion, yoga, psychotherapy, and neuromuscular electrical stimulation (NMES).[22–28] especially for NMES. However, limited data of NMES for the treatment of EAP have been reported presently. In this study, we retrospectively analyzed the effect and safety of NMES in patients with EAP.

2. Methods
This retrospective study was approved by the Medical Ethical Committee of The People’s Hospital of Yan’an. All patients had provided the written informed consent.

2.1. Design
This retrospective study was conducted at The People’s Hospital of Yan’an between January 2014 and December 2016. It included 154 female patients with EAP. All those subjects were divided into a treatment group and a control group according to the different interventions they received. Of those, 83 patients underwent NMES and were assigned to a treatment group, while other 71 patients were at waiting list and were assigned to a control group.

2.2. Patients
In this study, 154 eligible female patients aged from 18 to 42 years with confirmed diagnosis of EAP by a history of histological...
confirmed endometriosis and chronic pelvic pain were included. Patients were excluded if they were pregnancy, drug or alcohol addiction, and received medication and NMES or electroacupuncture within 1 month before this study.

2.3. Treatments

All 83 patients in the treatment group received NMES by using the NMES device (HANS-100; Nanjing Jisheng Medical Technology Co., Ltd, Nanjing, Jiangsu Province, China). It applied 2 gel pads attached to bilateral acupoints of Sanyinjiao (SP 6) (3 cun directly above the tip of the medial malleolus on the posterior border of the tibia), Zhongji (CV 3) (on the anterior median line of the lower abdomen, 4 cun below the belly button), and Guanyuan (CV 4) (on the anterior median line of the lower abdomen, 3 cun below the belly button) with 2 to 100 Hz for 30 minutes each session, once daily, 3 sessions weekly for a total of 10 weeks. The 71 patients in the control group were at waiting list and received no NMES therapy.

2.4. Outcome measurements

The primary outcome was pain, measured by the numerical rating scale (NRS).[25] The secondary outcome of quality of life was measured by the 36-Item Short Form Health Survey (SF-36).[1,3] It included 2 main subscales of Physical Component Summary (PCS) and Mental Component summary (MCS). It ranges from 0 to 100, with higher score indicating less disability.[31] All outcomes were measured before and after 5-week, and 10-week treatment. Moreover, all adverse events occurred in this study were documented.

2.5. Statistical analysis

All data were analyzed by using SPSS software (SPSS Version 19.0; IBM Corp., Armonk, NY). Continuous data were analyzed by the t test or Mann–Whitney rank sum test. Categorical data were analyzed by the Pearson Chi-square test or Fisher exact test. P < .05 was regarded as the statistical significance between the 2 groups.

3. Results

Patients’ characteristics of both groups at baseline are listed in Table 1. There are not significant differences in all characteristics between the 2 groups. These characteristics include age, race, weight, body mass index, and pain duration, stage of endometriosis, and patients with infertility, NRS, ESSS, SF-36, and previous analgesic medication used (Table 1).

After 5-week treatment, there are no significant differences in pain, measured by NRS (P = .14, Table 2), and ESSS (P = .12, Table 2), and quality of life, measured by SF-36 (PCS, P = .18; MCS, P = .21; Table 3) between the 2 groups.

After 10-week treatment, patients in the treatment group showed better effectiveness in NRS (P = .02, Table 2), ESSS (P = .04, Table 2), and SF-36 (PCS, P < .01; MCS, P < .01; Table 3), than the patients in the control group.

Adverse events are summarized in Table 4. No significant differences of all adverse events were found between 2 groups. Mild and acceptable adverse events occurred, and no severe adverse events were recorded in both groups.

4. Discussion

Presently, no study has specifically focused on investigating the efficacy and safety of NMES for the treatment of Chinese female patients with EAP. Previous related study explored the effect of psychotherapy-combined somatosensory stimulation for relieving EAP and improving quality of life in patients with EAP.[25] Its
results demonstrated that such therapy can either reduce global and pelvic pain, and dyschezia, or enhance quality of life in patients with endometriosis. After 6-month and 24-month treatment, all achieved stable improvements.\(^{[28]}\)

This study is the clinical study to specifically explore the effect and safety of NMES for treating Chinese patients with EAP. In this study, we utilized NMES for treating patients with EAP, compared with such kind of patients at waiting list. The results of this study did not find promising effect of NMES for EAP, assessed by the scales of NRS, ESS, PCS, and MCS after 5-week treatment. However, NMES exerts encouraging effect in either pain relief, measured by NMES and ESS, or quality of life improvement, measured by SF-36 (PCS and MCS) after 10-week treatment. In addition, only minor and acceptable adverse events occurred in this study.

Several limitations existed in this retrospective study. First, this study did not include placebo control group, because all data of this study were just based on the current available completed cases. Thus, this study only evaluates the effect, but not the efficacy of NMES for the treatment of EAP. Then, this study did not further assess the effect of NMES after 10-week treatment in longer term. Therefore, follow-up effectiveness evaluation should also be considered in the future study.

5. Conclusion

The results of this study showed that NMES is effective in female Chinese patients with EAP after 10-week treatment. Further studies are still needed to warrant this result.

Author contributions

Conceptualization: Cai-xia Xie, Xue-ling Bi.
Data curation: Cai-xia Xie, Xue-ling Bi.
Formal analysis: Xue-ling Bi.
Investigation: Xue-ling Bi.
Methodology: Xue-ling Bi.
Project administration: Cai-xia Xie, Xue-ling Bi.
Resources: Cai-xia Xie, Xue-ling Bi.
Software: Cai-xia Xie, Xue-ling Bi.

Supervision: Xue-ling Bi.
Validation: Cai-xia Xie.
Visualization: Cai-xia Xie.
Writing – original draft: Cai-xia Xie, Xue-ling Bi.
Writing – review & editing: Cai-xia Xie, Xue-ling Bi.

References

[1] Brown J, Farquhar C. An overview of treatments for endometriosis. JAMA 2015;313:296–7.
[2] Lu W, Chang CY, Hsu YA, et al. Increased risk of endometriosis in patients with lower genital tract infection: a nationwide cohort study. Medicine (Baltimore) 2016;95:e2773.
[3] Kodaman PH. Current strategies for endometriosis management. Obstet Gynecol Clin North Am 2015;42:87–101.
[4] Giudice LC. Endometriosis. N Engl J Med 2010;362:2389–98.
[5] Missmer SA, Hankinson SE, Speigelman D, et al. Reproductive history and endometriosis among premenopausal women. Obstet Gynecol 2004;104:965–74.
[6] Yauk JS, Park EJ, Soo YS, et al. Graves disease is associated with endometriosis: a 3-year population-based cross-sectional study. Medicine (Baltimore) 2016;95:e2975.
[7] Wei M, Cheng Y, Bu H, et al. Length of menstrual cycle and risk of endometriosis: a meta-analysis of 11 case-control studies. Medicine (Baltimore) 2016;95:e2922.
[8] Mihalovic A, Rottenstreich M, Kovel S, et al. Endometriosis-associated malignant transformation in abdominal surgical scar: a PRISMA-compliant systematic review. Medicine (Baltimore) 2017;96:e9136.
[9] Morotti M, Vincent K, Brawn J, et al. Peripheral changes in endometriosis-associated pain. Hum Reprod Update 2014;20:717–36.
[10] Ricci E, Viganò P, Cipriani S, et al. Physical activity and endometriosis risk in women with infertility or pain: systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e4957.
[11] Haydardedeooglu B, Zeyneloglu HB. The impact of endometriosis on fertility. Womens Health (Lond) 2015;11:619–23.
[12] Mavrelis D, Saridogan E. Treatment of endometriosis in women desiring fertility. J Obstet Gynaecol India 2015;65:11–6.
[13] Api M. Surgery for endometriosis-related pain. Womens Health (Lond) 2015;11:665–9.
[14] Gordis S, Koninckx P, Brosses I. Pathogenesis of deep endometriosis. Fertil Steril 2017;108:872–85.
[15] Pavone ME, Lytle BM. Endometriosis and ovarian cancer: links, risks, and challenges faced. Int J Womens Health 2015;7:663–72.
[16] Practice Committee of American Society for Reproductive Medicine. Treatment of pelvic pain associated with endometriosis. Fertil Steril 2008;90(suppl 5):S260–9.
[17] Bulun SE, Cheng YH, Pavone ME, et al. Estrogen receptor-beta, estrogen receptor-alpha, and progesterone resistance in endometriosis. Semin Reprod Med 2010;28:36–43.
[18] Crosignani PG, Luciano A, Ray A, et al. Subcutaneous depot medroxyprogesterone acetate versus leuprolide acetate in the treatment of endometriosis-associated pain. Hum Reprod 2006;21:248–56.
[19] Schlafli WD, Carson SA, Luciano A, et al. Subcutaneous injection of depot medroxyprogesterone acetate compared with leuprolide acetate in the treatment of endometriosis-associated pain. Fertil Steril 2006;85:314–25.
[20] Batzer FR. GnRH analogs: options for endometriosis-associated pain treatment. J Minim Invasive Gynecol 2006;13:539–45.
[21] Surrey ES. Gonadotropin-releasing hormone agonist and addback therapy: what do the data show? Curr Opin Obstet Gynecol 2010;22:283–8.
[22] Kong S, Zhang YH, Liu CF, et al. The complementary and alternative medicine for endometriosis: a review of utilization and mechanism. Evid Based Complement Alternat Med 2014;2014:146383.
[23] Leong FC. Complementary and alternative medications for chronic pelvic pain. Obstet Gynecol Clin North Am 2014;41:503–10.
[24] Gonçalves AV, Barros NF, Bahamondes L. The practice of hatha yoga for the treatment of pain associated with endometriosis. J Altern Complement Med 2017;23:45–52.
[25] Yan H, Huang XH, Deng GF. Observation on therapeutic effect of acupuncture and moxibustion on disorders of myometrial gland. Zhongguo Zhen Jiu 2008;28:579–81.
[26] Chen M, Zhang H, Li J, et al. Clinical observation on acupuncture combined with acupoint sticking therapy for treatment of dysmenorrhea caused by endometriosis. Zhongguo Zhen Jiu 2010;30:725–8.
[27] Zhang XY, Zhang CY. Efficacy observation on the combination of acupuncture and Chinese medication in prevention of the recurrence of endometriosis after laparoscopic surgery. Zhongguo Zhen Jiu 2014;34:139–44.
[28] Meissner K, Schweizer-Arau A, Limmer A, et al. Psychotherapy with somatosensory stimulation for endometriosis-associated pain: a randomized controlled trial. Obstet Gynecol 2016;128:1134–42.
[29] Lee JJ, Lee MK, Kim JE, et al. Pain relief scale is more highly correlated with numerical rating scale than with visual analogue scale in chronic pain patients. Pain Physician 2015;18:E195–200.
[30] Miller JD. Quantification of endometriosis-associated pain and quality of life during the stimulatory phase of gonadotropin-releasing hormone agonist therapy: a double-blind, randomized, placebo-controlled trial. Am J Obstet Gynecol 2000;182:1483–8.
[31] Larson JS. The MOS 36-item short form health survey. A conceptual analysis. Eval Health Prof 1997;20:14–27.