European Journal of Obstetrics & Gynecology and Reproductive Biology 194 (2015) 1–6

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Effectiveness of complementary pain treatment for women with deep endometriosis through Transcutaneous Electrical Nerve Stimulation (TENS): randomized controlled trial

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ARTICLE INFO

Article history:
Received 25 February 2015
Received in revised form 3 July 2015
Accepted 23 July 2015

Keywords:
Transcutaneous Electrical Nerve Stimulation
Endometriosis
Chronic pelvic pain
Dyspareunia
Physical therapy

ABSTRACT

Objective: Evaluate TENS effectiveness as a complementary treatment of chronic pelvic pain and deep dyspareunia in women with deep endometriosis.
Study design: This randomized controlled trial was performed in a tertiary health care center, including twenty-two women with deep endometriosis undergoing hormone therapy with persistent pelvic pain and/or deep dyspareunia. This study was registered in the Brazilian Record of Clinical Trials (ReBEC), under n RBR-3rndh6. TENS application for 8 weeks followed a randomized allocation into two groups: Group 1 – acupuncture-like TENS (Frequency: 8 Hz, pulse duration: 250 μs) – VIF ($n = 11$) and Group 2 – self-applied TENS (Frequency: 85 Hz, pulse duration: 75 μs) ($n = 11$). The intensity applied was "strong, but comfortable". We evaluated patients before and after treatment by the use of the Visual Analogue Scale, Deep Dyspareunia Scale and Endometriosis Quality of Life Questionnaire. We used the Wilcoxon and Mann–Whitney tests to compare before and after treatment conditions.
Results: Despite the use of hormone therapy for 1.65 ± 2.08 years, the 22 women with deep endometriosis sustained pelvic pain complaints (VAS = 5.95 ± 2.13 and 2.45 ± 2.42, $p < .001$) and/or deep dyspareunia (DDS = 2.29 ± 0.46 and 1.20 ± 1.01, $p = .001$). We observed significant improvement for chronic pelvic pain, deep dyspareunia and quality of life by the use of TENS. Both application types of TENS were effective for improving the evaluated types of pain.
Conclusions: Both resources (acupuncture-like TENS and self-applied TENS) demonstrated effectiveness as a complementary treatment of pelvic pain and deep dyspareunia, improving quality of life in women with deep endometriosis regardless of the device used for treatment.
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Introduction

Endometriosis is a chronic estrogen-dependent inflammatory disease, affecting 5–15% of women in reproductive age, causing infertility and pain. Pain complaints are manifested as chronic pelvic pain, deep dyspareunia, and also dysmenorrhea, dyschezia and dysuria [1–5]. The most used treatment is surgical excision as well the use of drugs that can block the production or action of estrogens [6–8]. Although their use may have positive effects, many women continue suffering from pain. There is scarce literature on the use of complementary therapy for pain management, and acupuncture and exercises are the most commonly proposed alternatives [9–13].

Electrotherapy can treat diverse symptoms produced by diseases that affect the human body. Electrotherapy using Transcutaneous Electrical Nerve Stimulation (TENS) is a low-cost, non-invasive and easily accessible technique to treat pain [14,15]. TENS acts by spinal blocking and endogenous opioids release [16,17]. Its parameters may be adjusted, widening its range of action on pain [18]. Recent technological advances facilitated the use of self-applied TENS devices [19]. In this context, numerous descriptions emerge on the effectiveness of TENS for treating diverse types of pain (e.g. chronic low back pain, knee osteoarthritis, and dysmenorrhea) [20–24]. However, there are no specific studies on pain caused by endometriosis.

The aim of this study was to primarily evaluating the effectiveness of electrotherapy with TENS as a complementary treatment of pelvic pain and/or deep dyspareunia, as well its impact on quality of life of women suffering from deep endometriosis with persistent pain complaints, despite the use of hormone therapy.

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http://dx.doi.org/10.1016/j.ejogrb.2015.07.009
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Escore	Description
0	No pain during the intercourse
1	Mild pain, which does not require interruption of the intercourse
2	Moderate pain, which does not require interruption of the intercourse, but difficulted it
3	Intense pain, which requires interruption of the intercourse

Fig. 1. Deep Dyspareunia Scale specifically elaborated for this study and based on the penetration dyspareunia scale created by Marinoff.

Materials and methods

We performed a non-blind, randomized clinical trial, including 22 women with deep endometriosis diagnosed in the cul-de-sac and intestinal loop who sustained pelvic pain and/or deep dyspareunia, despite continuous clinical medication. Participants received intervention and were randomized into two groups: Group 1 – acupuncture-like TENS (Dualpex 961®) ($n = 11$) and Group 2 – self-applied TENS (Tanyx®) ($n = 11$). We applied TENS at the S3–S4 region for both groups. This region is related to the sacral plexus and communicates with the pelvic splanchnic and inferior hypogastric plexus, which are responsible for pelvic structures innervation. The study was conducted in the Women's Hospital of the University of Campinas. This study was approved by the Research Ethics Committee of the institution and recorded in the Brazilian Record of Clinical Trials (ReBEC), RBR-3rndh6. All women signed a consent term before inclusion.

Women were recruited through their medical records and also during routine consultation at the Endometriosis Outpatient Facility from November 2013 to June 2014. Inclusion criteria: women at menacme, ranging from 18 to 50 years-old, diagnosed with deep endometriosis in the cul-de-sac and/or intestinal loop using imaging tests with ultrasonography after bowel preparation. The exam was performed by a single specialized ultrasonographist. All women were undergoing hormone therapy with continuous progestin alone or combined oral contraceptives for at least three months, reporting pelvic pain and/or deep dyspareunia persistence, associated or not with other pain complaints (dysmenorrhea, dyschezia and dysuria). Exclusion criteria: women with decreased skin sensitivity, implanted with a pacemaker, skin hypersensitivity (allergic reactions to gel or electrodes), epilepsy, heart disease (cardiac arrhythmia), osteosynthesis in the region of application, full-thickness defects of the skin, malignant tumors, acute inflammatory disease, and cognitive deficiency that precluded comprehension of the instruments in this study.

Randomization was generated by a computer program. Opaque sealed envelopes were used for participant randomized allocation into the two groups. Both processes were performed by a person who did not participated in the study.

All study participants responded to the Visual Analogue Scale [26,27] for quantification of pain complaints (chronic pelvic pain, dyschezia, dysuria and dysmenorrhea). We evaluated pain characteristics according to sexual intercourse pain (deep dyspareunia) in response to the Deep Dyspareunia Scale, specifically elaborated for this study and based on the penetration dyspareunia scale created by Marinoff. Fig. 1 shows our scale grading.

A quantitative measurement on quality of life impact was performed by using the Endometriosis Health Profile (EHP-30) [28], which was validated for the Portuguese language [29]. The instrument has 53 questions, divided into two parts: general information (pain, control/powerlessness, emotional well-being, social support and self-image) and specific information (work, intercourse, relationship with children, medical profession, treatment and infertility). The better the quality of life the lower the total score. All instruments were applied before and after treatment. Table 1 describes a summary of all application methods and interventions applied.

Since there were no previous studies using TENS to treat endometriosis and pain in women, the sample size was calculated based on a study by Wang, Lee and Hwa (2009). Those authors evaluated TENS by administering the Visual Analogue Scale in women with primary dysmenorrhea [30]. TENS treatment obtained a sample size of 16 patients, with a 90% test power and 5% significance level. Considering a 20% loss during follow-up, the total sample size achieved was 20 women, equally distributed between the two groups.

The Fisher's exact test measured group differences. The paired Wilcoxon test compared quantitative variables before and after treatment. Mann–Whitney test compared variables between groups. We assumed p-values <0.05 as statistically significant.

Results

Table 2 shows demographic and clinical characteristics. Fig. 2 shows an eligibility summary for our clinical trial at a Flow Chart for Randomized Controlled Trials [25].

The main sites of pain pointed by women were suprapubic (22%), sacral (9%) and in both regions in association in 69% of them.

Table 1
Summary of the applied application methods and interventions (acupuncture and self-applied TENS).

	Acupuncture-like TENS	Self-applied TENS
Protocol	*Frequency*: 8 Hz *Pulse duration*: ~250 μs and VIF (variation in intensity and frequency of 1 ms) *Intensity*: adjusted according to the woman ("strong, but comfortable") without any motor stimulation. *Application site*: sacral region (S3–S4). *Method*: A dual-channel TENS unit was used, equipped with four rubber electrodes (~5 cm × 3 cm) and neutral aqueous gel lubricant, attached to the skin with adhesive tape crossed in an "X" pattern. *Time*: 30 min and sessions were performed once a week, for a period of 8 weeks.	*Frequency*: 85 Hz *Pulse duration*: ~75 μs *Intensity*: adjustable in three options: 10, 20 or 30 mA. Women were instructed to choose the intensity that was "strong, but comfortable" *Application site*: sacral region (S3–S4). *Method*: The correct placement of the device was initially explained and demonstrated on the patient during evaluation, and doubts were dispelled by the researcher. TENS application was performed at home by the patient herself. She could follow instructions from a didactic illustration showing the exposed sacral region of a supine woman next to another illustration of the same woman with the equipment in place. *Time*: Twice a day, 20 min per application, setting an interval of 12 h between applications. A return visit was scheduled after four weeks of treatment for follow-up of the use of the device. A final reassessment was carried out after 8 weeks.

Table 2
Total and separated groups (acupuncture and self-applied TENS) demographic and clinical characteristics.

Demographic and clinical characteristics	Total group ($n = 22$) (Mean ± SD)	Acupuncture-like TENS ($n = 11$) (Mean ± SD)	Self-applied TENS ($n = 11$) (Mean ± SD)	p value*
Age (years)	36.0 ± 7.1	41.0 ± 5.4	30.9 ± 4.5	*.002*
Age of the onset of symptoms (years)	21.0 ± 5.7	20.6 ± 5.7	21.3 ± 6.0	.91
Age of the diagnosis of endometriosis (years)	29.1 ± 7.8	32.5 ± 9.0	25.8 ± 4.9	.12
Body mass index (kg/m^2)	26.4 ± 4.7	26.3 ± 4.2	26.5 ± 5.3	.89
School education (years)	13.8 ± 2.7	13.8 ± 2.9	13.8 ± 2.7	1.00
Time of use of hormone therapy (years)	1.6 ± 2.08	1.8 ± 2.7	1.4 ± 1.1	.94
Number of surgeries (per women)	2.3 ± 2.0	2.6 ± 1.9	2.0 ± 2.2	.29
Live with partner (%)	81.8	90.0	72.7	
Employed (%)	81.8	81.9	91.0	
Practicing physical activity (%)	50.0	54.5	45.5	
Medicines				
Progestin (%) (Desogestrel; Levonorgestrel intrauterine device; Dienogest; Medroxyprogesterone acetate depot)	86.3	90.9	81.8	
Combined oral contraceptives (%) (Gestodene + Ethinylestradiol; Desogestrel + Ethinylestradiol)	13.6	9.1	18.2	

Fisher's exact test.
* Comparative analysis between acupuncture-like TENS and Self-applied TENS.

The reported pain profile can be summarized by acute pain/cramps (45.5%), needle or burning (36.3%), throbbing, stabbing or impressive (40.9%) and other pains (22.7%). For some women those complaints were associated.

For all women, TENS provided symptomatic pain relief, with significant differences before and after chronic pelvic pain treatment ($p < .0001$), deep dyspareunia ($p = .001$) and dyschezia ($p = .001$) in women with deep endometriosis (cul-de-sac and intestinal loop).

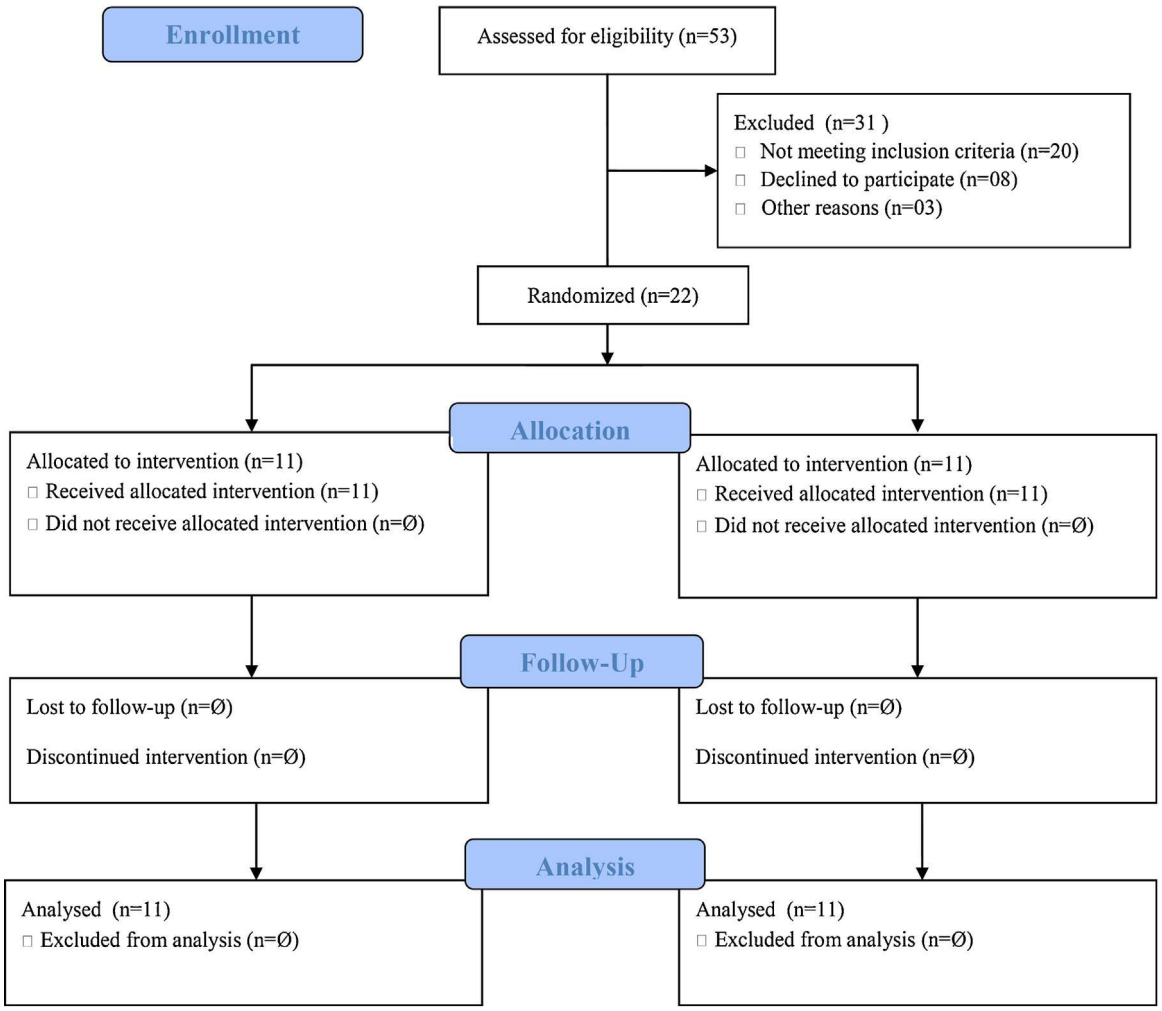

Fig. 2. Summary of our clinical trial at the Flow Chart for Randomized Controlled Trials (CONSORT).

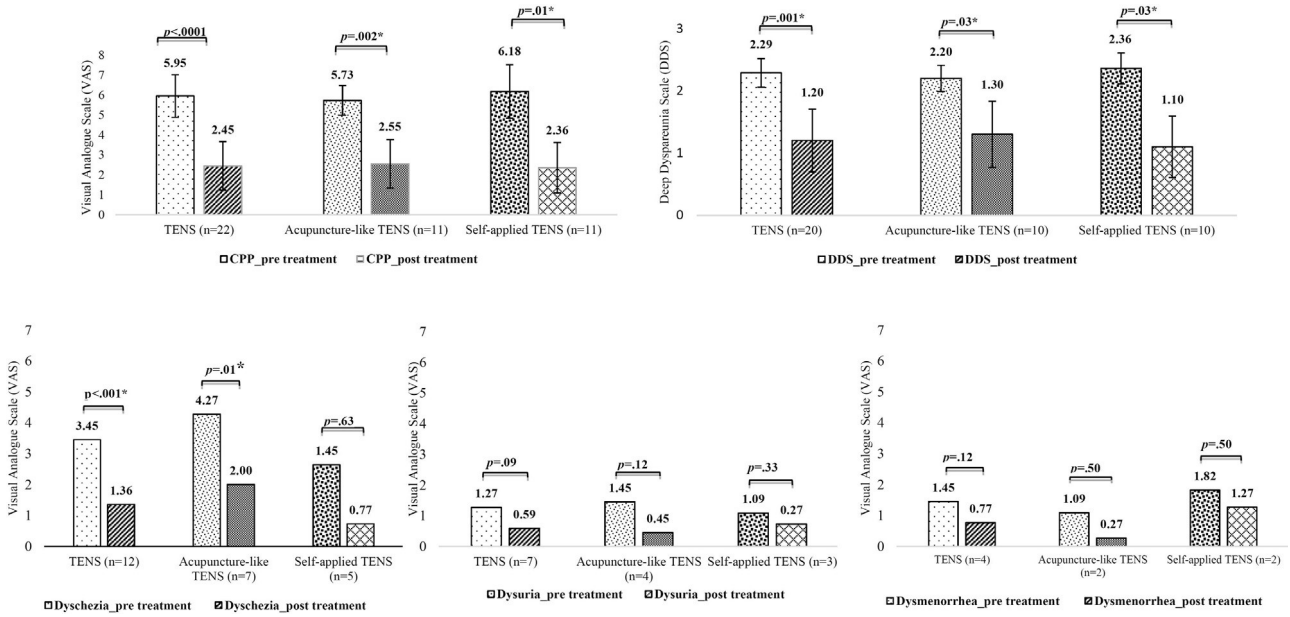

Fig. 3. Evaluation of the chronic pelvic pain, dyschezia, dysuria and dysmenorrhea by Visual Analogue Scale (VAS) and deep dyspareunia by Deep Dyspareunia Scale (DDS), pre and post complementary treatment using Transcutaneous Electrical Nerve Stimulation (TENS).

However, there was no improvement for dysmenorrhea ($p = .12$) and dysuria ($p = .09$) (Fig. 3).

Improvements in quality of life covers general questions with significantly reduced scores for pain domains ($p = .01$), and control and powerlessness in the presence of endometriosis ($p < .0001$); Furthermore, the participants reported improvement in emotional well-being ($p < .0001$), social support ($p = .01$) and self-image ($p = .01$) (Table 3).

For quality of life specific assessment through the EHP-30 questionnaire, TENS improved aspects related to the work domain ($p = .03$), sexual intercourse ($p < .0001$) and treatment ($p < .0001$), with reflections on the modular questionnaire's final score ($p < .0001$). The total EHP-30 score significant reduced ($p < .0001$) indicating that complementary treatment with TENS had a positive impact, improving quality of life (Table 3).

We also observed chronic pelvic pain relief ($p = .002$ and $p = .01$) and deep dyspareunia ($p = .03$ and $p = .03$) for both types of TENS (acupuncture-like and self-applied), without differences between them. Pain relief during defecation was observed only with the use of acupuncture-like TENS ($p = .01$) (Fig. 3). Indirect evaluation of pain relief, through the influence of symptoms on quality of life, showed that both modes of TENS had a positive impact, improving various aspects analyzed. When both types of TENS were compared together in terms of different pain complaints improvement, no difference was observed between acupuncture-like and self-applied TENS (Table 4).

Table 3
Quality of life evaluation by Endometriosis Health Profile (EHP-30) of the total group, pre and post complementary treatment using Transcutaneous Electrical Nerve Stimulation (TENS).

Quality of life (EHP-30)	TENS treatment ($n = 22$)		
	Pre (mean ± SD)	Post (mean ± SD)	p value
Core questionnaire			
Pain	13.47 ± 4.28	9.69 ± 4.61	.01
Control and powerlessness	6.67 ± 2.00	4.16 ± 2.16	<.0001
Emotional well being	7.12 ± 2.04	4.99 ± 1.94	<.0001
Social support	4.65 ± 1.38	3.66 ± 1.66	.01
Self-image	2.92 ± 1.46	2.37 ± 1.33	.01
Core score	34.82 ± 8.92	24.87 ± 9.69	<.0001
Modular questionnaire			
Work	3.13 ± 2.74	2.26 ± 1.86	.03
Intercourse	7.24 ± 2.09	4.82 ± 2.60	<.0001
Relationship with children	0.76 ± 1.02	0.64 ± 0.90	.57
Medical profession	2.90 ± 1.41	2.33 ± 1.55	.01
Treatment	2.88 ± 1.08	1.88 ± 1.08	<.0001
Infertility	2.85 ± 2.79	2.68 ± 2.49	.54
Modular score	19.76 ± 4.92	14.61 ± 5.67	<.0001
Total score	54.58 ± 12.10	39.49 ± 13.60	<.0001

Paired Wilcoxon test.

Comments

Our results demonstrated the effectiveness of acupuncture-like TENS and self-applied TENS as complementary treatment of chronic pelvic pain and deep dyspareunia in women suffering from deep endometriosis with intractable pain, despite the use of hormone therapy. Furthermore, we observed a significant benefit in all considered aspects by the applied questionnaire on quality of life. Both types of TENS (acupuncture-like and self-applied modes), were comparable in terms of pain relief and improvement in quality of life.

As far as we know, our randomized clinical trial was the first to evaluate the use of TENS as a complementary treatment of pain, specifically related to deep endometriosis. It is known that despite the different types of hormone therapy used, many women who suffer from endometriosis sustain pain negatively reflecting on their quality of life. This complementary treatment may represent an important adjunct alternative for these women, however, there is still insufficient solid scientific evidence to prove its effectiveness.

Positive results have been found in the relief of chronic pelvic pain due to idiopathic or other causes, with the use of Percutaneous Tibial Nerve Stimulation or intravaginal TENS [31,32]. The Consensus of Endometriosis [8] cites TENS as a therapeutic option for pain, based on a review by Proctor et al. concerning dysmenorrhea in general [33]. Particularly for endometriosis, studies with acupuncture and exercises have also shown positive results for pain relief [9–13].

Our study included a small number of women: all with deep endometriosis. In severe cases they had no satisfactory response to hormone therapy and the pain relief caused by TENS determined a

Table 4
Quality of life evaluation by Endometriosis Health Profile (EHP-30) of the acupuncture and self-applied TENS groups, pre and post complementary treatment using Transcutaneous Electrical Nerve Stimulation (TENS).

	Acupuncture-like TENS ($n = 11$)			Self-applied TENS ($n = 11$)			G1 × G2[†]
	Pre (mean ± SD)	Post (mean ± SD)	p value[*]	Pre (mean ± SD)	Post (mean ± SD)	p value[*]	
Quality of life (EHP-30)							
Core questionnaire							
Pain	11.60 ± 3.23	7.46 ± 2.89	.01	15.33 ± 4.51	11.91 ± 5.05	.05	.40
Control and powerlessness	5.91 ± 2.32	3.35 ± 1.50	.001	7.43 ± 1.31	4.97 ± 2.47	.003	.92
Emotional well being	6.18 ± 2.02	4.32 ± 1.62	.004	8.05 ± 1.65	5.67 ± 2.07	.002	.30
Social support	4.53 ± 1.52	3.25 ± 1.60	.002	4.77 ± 1.28	4.08 ± 1.68	.28	.84
Self-image	2.42 ± 1.56	1.90 ± 1.06	.17	3.42 ± 1.21	2.83 ± 1.46	.05	.36
Core score	30.64 ± 8.75	20.28 ± 6.38	.002	39.00 ± 7.23	29.47 ± 10.49	.01	.79
Modular questionnaire							
Work	2.90 ± 1.50	1.90 ± 1.11	.07	3.35 ± 3.66	2.63 ± 2.40	.43	.81
Intercourse	0.90 ± 0.80	0.86 ± 0.87	1.00	0.62 ± 1.22	0.41 ± 0.92	1.00	1.00
Relationship with children	6.74 ± 2.64	4.08 ± 2.17	.003	7.74 ± 1.29	5.56 ± 2.87	.01	.47
Medical profession	3.01 ± 1.41	1.86 ± 1.02	.01	2.80 ± 1.46	2.80 ± 1.87	.86	.06
Treatment	2.87 ± 1.17	1.83 ± 1.34	.02	2.90 ± 1.04	1.93 ± 0.82	.003	.55
Infertility	0.93 ± 1.73	1.28 ± 1.74	.75	4.77 ± 2.29	4.08 ± 2.39	.153	.16
Modular score	17.34 ± 4.16	11.81 ± 3.97	.002	22.18 ± 4.53	17.41 ± 5.88	.04	.56
Total score	47.98 ± 11.18	32.09 ± 8.65	.002	61.18 ± 9.32	46.88 ± 13.91	.01	.79

[*] p value for comparison before and after treatment. Paired Wilcoxon test.
[†] Comparative analysis between improvement in scores before and after treatment for groups G1 × G2. Mann–Whitney test.

relevant outcome. The replication of this study with a larger number of women may potentially guide non-invasive treatments, decreasing surgical indications [34] and probably, the repetition of surgical procedures.

Both high and low-frequency TENS act on the spinal column dorsal horn, where it releases circulating endogenous opioids, particularly β-endorphin. They relieve pain during the delivery of the electrical current producing analgesia that lasts from minutes to hours [35]. It is known that repeated TENS application results in a cumulative effect, with a longer pain relief. This may explain our findings, showing pain relief throughout a 8 weeks protocol. It is worth reinforcing that variation in intensity and frequency (VIF), present in acupuncture-like TENS used in this study, acts by preventing opioid tolerance generated by a equal intensity current during a prolonged period of electrostimulation [36,37]. On the other hand, variation in intensity and frequency is not included in the self-applied TENS device. Despite this, tolerance did not interfere in our results, since women who used this TENS mode also experienced pain reduction, without any differences between groups.

Deep dyspareunia is a symptom that until now has not been fully evaluated. Hormone therapy used in endometriosis is known to offer positive perspectives in pain relief during intercourse [7,38]. When pain relief fails, the clinical resources available are quite limited. We observed improvements with the use of TENS, regardless the used mode. We found no scientific studies for comparison. There are only reports on deep dyspareunia improvement with TENS, but no specific study directly dealing with endometriosis [39,40].

Some women included in the study reported complaints about dyschezia, dysuria and dysmenorrhea. Dyschezia was significantly alleviated in the group using acupuncture-like TENS. Pain relief in TENS may be related to the region of application, improving peristaltic movements by sympathetic nervous system stimulation [41]. These results were only manifested in the acupuncture-like TENS group probably because of the number of women with these symptoms. Thus, it is important to highlight that these secondary findings are limited by the number of women in group 1. Our study does not permit making conclusions about the reflections of TENS administration on dysmenorrhea and dysuria, due to its low frequency. In fact, dysmenorrhea is limited to irregular episodes and eventual bleeding in women using continuous hormone therapy.

It is well-known that endometriosis is a chronic disease with a negative impact on quality of life [32,42]. The chance of improving the quality of life by pain relief reinforces the indication of complementary resources for pain treatment. The use of acupuncture-like TENS and self-applied TENS had positive repercussions on various aspects of quality of life. Thus, pain relief was probably a decisive factor for the decrease in feelings of powerlessness due to endometriosis, improved emotional and social well-being and improvement in self-image of these women. Thus, we may consider that pain reduction improved their working capacity, as well as her sexual performance. Finally, the quality of life of those women improved, which was the main aim of treating a chronic and non-curable disease.

We should also consider that self-applied TENS is characterized as being an easy method to use at home, offering greater convenience and easy-of-access to the patient. In contrast, acupuncture-like TENS permits contact with the physical therapist during application and may have influenced the results observed in some domains of quality of life.

Some weaknesses must be cited, such as the follow-up period of these women, sample size and lack of a placebo TENS group serving as control. The positive results obtained regarding such significant complaints justifies further studies to evaluate the use of other electrotherapeutic resources as complementary treatment for endometriosis.

In conclusion, TENS was beneficial as a complementary treatment of chronic pelvic pain and deep dyspareunia in women with deep endometriosis with improvement in quality of life. The effectiveness of a non-invasive electrotherapeutic resource in alleviating pelvic pain and improving quality of life justifies its use and prescription.

Acknowledgment

This study was partially funded by the Research Support Foundation of the State of São Paulo (FAPESP), process n 2013/11790-2.

References

[1] Dizereza GS, Barber DL, Hodgen GD. Endometriosis: role of ovarian steroids in initiation, maintenance, and suppression. Fertil Steril 1980;33(6):649–53. PMID: 6769717.

[2] Kennedy S, Bergqvist A, Chapron C, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod 2005;20(10):2698–704. PMID: 15980014.

[3] Ferrero S, Esposito F, Abbamonte LH, Anserini P, Remorgida V, Rogni N. Quality of sex life in women with endometriosis and deep dyspareunia. Fertil Steril 2005;83(3):573–9. PMID: 15749483.

[4] Amer S, Endometriosis. Obstet Gynecol Reprod Med 2008;18(5):126–33.

[5] Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. Fertil Steril 2012;98(3):511–9. http://dx.doi.org/10.1016/j.fertnstert.2012.06.029 [Epub 2012 Jul 20].

[6] Chwalisz K, Brenner RM, Fuhrmann UU, Hess-Stumpp H, Elger W. Antiproliferative effects of progesterone antagonists and progesterone receptor modulators on the endometrium. Steroids 2000;65(10–11):741–51. PMID: 11108885.

[7] Vercellini P, Frattaruolo MP, Somigliana E, et al. Surgical versus low-dose progestin treatment for endometriosis-associated severe deep dyspareunia II: Effect on sexual functioning, psychological status and health-related quality of life. Hum Reprod 2013;28(5):1221–30. http://dx.doi.org/10.1093/humrep/det041 [Epub 2013 Feb 26].

[8] Johnson NP, Hummelshoj L. Consensus on current management of endometriosis. Hum Reprod 2013;28(6):1552–68. http://dx.doi.org/10.1093/humrep/det050 [Epub 2013 Mar 25].

[9] Carpenter SE, Tjaden B, Rock JA, Kimball A. The effect of regular exercise on women receiving danazol for treatment of endometriosis. Int J Gynaecol Obstet 1995;49(3):299–304. PMID: 9764869.

[10] Yu F, Tian X. Clinical observation on treatment of endometriosis with acupuncture plus herbs. J Acupunct Tuina Sci 2005;3(5):48–51.

[11] Wayne PM, Kerr CE, Schnyer RN, et al. Japanese-style acupuncture for endometriosis-related pelvic pain in adolescents and young women: results of randomized sham-controlled trial. J Pediatr Adolesc Gynecol 2008;21(5):247–57. http://dx.doi.org/10.1016/j.jpag.2007.07.008.

[12] Rubi-Klein K, Kucera-Sliutz E, Nissel H, et al. Is acupuncture in addition to conventional medicine effective as pain treatment for endometriosis? A randomized controlled cross-over trial. Eur J Obstet Gynecol Reprod Biol 2010;153(1):90–3. http://dx.doi.org/10.1016/j.ejogrb.2010.06.023 [Epub 2010 Aug 21].

[13] Zhao L, Wu H, Zhou X, Wang Q, Zhu W, Chen J. Effects of progressive muscular relaxation training on anxiety, depression and quality of life of endometriosis patients under gonadotrophin-releasing hormone agonist therapy. Eur J Obstet Gynecol Reprod Biol 2012;162(2):211–5. http://dx.doi.org/10.1016/j.ejogrb.2012.02.029 [Epub 2012 Mar 26].

[14] Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965;150(3699):971–9. PMID: 5320816.

[15] Radhakrishnan R, Sluka KA. Spinal muscarinic receptors are activated during low or high frequency TENS-induced antihyperalgesia in rats. Neuropharmacology 2003;45(8):1111–9. PMID: 14614954.

[16] Melzack R. From the gate to the neuromatrix. Pain 1999;6:S121–6. PMID: 10491980.

[17] Sluka KA. The basic science mechanisms of TENS and clinical implications. Am Pain Soc 2001;11(2):1–8.

[18] Walsh D, Tracey H, Johnson MI, Fidelma M, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. Cochrane Database Syst Rev 2009;2:CD006142.

[19] Pallet EJ, Rentowl P, Watson PJ. Validation of two novel electronic devices to time-link transcutaneous electrical nerve stimulation and pain report in patients with chronic back pain. Clin J Pain 2013;29(1):35–42. http://dx.doi.org/10.1097/AJP.0b013e31824781d8.

[20] Mankovsky-Arnold T, Wideman TH, Larivière C, Sullivan MJL. TENS attenuates repetition-induced summation of activity-related pain following experimentally induced muscle soreness. J Pain 2013;14(11):1416–24. http://dx.doi.org/10.1016/j.jpain.2013.07.019.

[21] Chen WL, Hsu WC, Lin YJ, Hsieh LF. Comparison of intra-articular acid injections with transcutaneous electric nerve stimulation for the management of knee osteoarthritis: a randomized controlled trial. Arch Phys Med Rehabil 2013;94(8):1482–9. http://dx.doi.org/10.1016/j.apmr.2013.04.009 [Epub 2013 Apr 27].

[22] Dailey DL, Rakel BA, Vance CGT, et al. Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. Pain 2013;154(11):2554–62. http://dx.doi.org/10.1016/j.pain.2013.07.043 [Epub 2013 Jul 27].

[23] Tokuda M, Tabira K, Masuda T, Nishiwada T, Shomoto K. Effect of modulated-frequency and modulated-intensity transcutaneous electrical nerve stimulation after abdominal surgery: a randomized controlled trial. Clin J Pain 2014;30(7):565–70. http://dx.doi.org/10.1097/AJP.0b013e31829a151.

[24] Chen YW, Tzeng JI, Lin MF, Hung CH, Hsieh PL, Wang JJ. High-frequency transcutaneous electrical nerve stimulation attenuates postsurgical pain and inhibits excess substance P in rat dorsal root ganglion. Reg Anesth Pain Med 2014;39(4):322–8. http://dx.doi.org/10.1097/AAP.0000000000000091.

[25] Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med 2010;152(11):726–32. http://dx.doi.org/10.7326/0003-4819-152-11-201006010-00232 [Epub 2010 Mar 24].

[26] Scott J, Huskisson EC. Graphic representation of pain. Pain 1976;2(2):175–84. PMID: 1026900.

[27] Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain 1997;72(1–2):95–7. PMID: 9272792.

[28] Jones GMA, Kennedy SMD, Bernard A, Wong JPD, Jenkinson CD. Development of a endometriosis quality-of-life instrument: The Endometriosis Health Profile-30. Obstet Gynecol 2001;98(2):258–64. PMID: 11506842.

[29] Mengarda CV, Passos EP, Picon P, Costa AF, Picon PD. Validation of Brazilian Portuguese version of quality of life questionnaire for women with endometriosis (Endometriosis Health Profile Questionnaire – EHP-30). Rev Bras Ginecol Obstet 2008;30(8):384–92. PMID: 19142521.

[30] Wang SF, Lee JP, Hwa HL. Effect of transcutaneous electrical nerve stimulation on primary dysmenorrhea. Neuromodulation 2009;12(4):302–9. http://dx.doi.org/10.1111/j.1525-1403.2009.00226.x [Epub 2009 Aug 20].

[31] Istek A, Ugurlucan FG, Yasa C, Gokyildiz S, Yalcin O. Randomized trial of long-term effects of percutaneous tibial nerve stimulation on chronic pelvic pain. Arch Gynecol Obstet 2014;290(2):291–8. http://dx.doi.org/10.1007/s00404-014-3190-z [Epub 2014 Mar 12].

[32] de Bernardes NO, Marques A, Ganunny C, Bahamondes L. Randomized double-blind crossover clinical trial on the use of intravaginal electrical stimulation for treatment of chronic pelvic pain. J Reprod Med 2010;55(1–2):19–24. PMID: 20337203.

[33] Proctor M, Farquhar C, Stones W, He L, Zhu X, Brown J. Transcutaneous electrical nerve stimulation for primary dysmenorrhea. Cochrane Database Syst Rev 2002;1:CD002123. PMID: 11869624.

[34] Lower AM, Hawthorn RJ, Clark D, et al. Adhesion-related readmissions following gynaecological laparoscopy or laparotomy in Scotland: an epidemiological study of 24 046 patients. Hum Reprod 2004;19(8):1877–85. PMID: 15178659.

[35] Sluka KA, Bjordal JM, Marchand S, Rakel BA. What makes transcutaneous electrical nerve stimulation work? Making sense of the mixed results in the clinical literature. Phys Ther 2013;93(10):1397–402. http://dx.doi.org/10.2522/ptj.20120281 [Epub 2013 May 2].

[36] deSantana JM, Santana-Filho VJ, Sluka KA. Modulation between high- and low-frequency transcutaneous electrical nerve stimulation delays the development of analgesic tolerance in arthritic rats. Arch Phys Med Rehabil 2008;89:754–60. http://dx.doi.org/10.1016/j.apmr.2007.11.027.

[37] Sato KL, Sanada LS, Rakel BA, Sluka KA. Increasing intensity of TENS prevents analgesic tolerance in rats. J Pain 2012;13(9):884–90. http://dx.doi.org/10.1016/j.jpain.2012.06.004 [Epub 2012 Aug 1].

[38] Vercellini P, Somigliana E, Consonni D, Frattaruolo MP, De Giorgi O, Fedele L. Surgical versus medical treatment for endometriosis-associated severe deep dyspareunia. I: Effect on pain during intercourse and patient satisfaction. Hum Reprod 2012;27(12):3450–9. http://dx.doi.org/10.1093/humrep/des313 [Epub 2012 Aug 27].

[39] Murina F, Graziottin A, Felice R, Radici G, Tognocchi C. Vestibulodynia: synergy between palmitoylethanolamide + transpolydatin and transcutaneous electrical nerve stimulation. J Low Genit Tract Dis 2013;17(2):111–6. http://dx.doi.org/10.1097/LGT.0b013e3182652316.

[40] Dionisi B, Senatori R. Effect of transcutaneous electrical nerve stimulation on the postpartum dyspareunia treatment. J Obstet Gynaecol Res 2011;37(7):750–3. http://dx.doi.org/10.1111/j.1447-0756.2010.01425.x [Epub 2011 Mar 13].

[41] Kamm MA, Dudding TC, Melenhorst J, et al. Sacral nerve stimulation for intractable constipation. Gut 2010;59:333–40. http://dx.doi.org/10.1136/gut.2009.187989.

[42] Minson FP, Abrão MS, Sardá Junior J, Kraychete DC, Podgaec S, Assis FD. Importance of quality of life assessment in patients with endometriosis. Rev Bras Ginecol Obstet 2012;34(1):11–5. PMID: 22358342.