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Ashley M. Hayes

*Philadelphia College of Osteopathic Medicine*

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**Is acupuncture effective in improving the quality of life for women  
in the reproductive age diagnosed with endometriosis?**

Ashley M. Hayes, PA-S

A SELECTIVE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences– Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
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## ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not acupuncture is effective in improving the quality of life for women in the reproductive age diagnosed with endometriosis.

Study Design: Review of 3 RCTs published between 2011-current, all in the English language. One of the RCTs was blinded while the other two were non-blinded.

Data Source: Three RCTs that analyzed the effectiveness of acupuncture therapy compared to control groups. All studies were found using EBSCOhost, PubMed and Medline and were selected based on relevance to the proposed clinical question.

Outcomes Measured: Each of the 3 articles analyzed the effectiveness of improving the quality of life for women in the reproductive age diagnosed with endometriosis. The Endometriosis Health Profile 30 and the physical and psychological sum score of the German version of the 12-Item Short-Form Health Survey were tools used to measure quality of life. The significance of the outcomes was determined using ANOVA p-value, Paired Wilcox test, paired t test, mean change, standard deviation and average.

Results: All 3 studies showed a significant improvement in the quality of life following treatment with acupuncture. de Sousa TR et al found a statistically significant increase in quality of life after 5 sessions of acupuncture compared to those that received the placebo acupuncture.<sup>2</sup> Meissner K et al found a statistically significant increase in the quality of life in the intervention group at 3 months.<sup>5</sup> However, at the 6-month follow-up the control group had a statistically significant increase in the quality of life compared to the intervention group.<sup>5</sup> Mira T A et al also found a statistically significant increase in the quality of life of women with endometriosis after acupuncture treatment, but it was in both types of groups (acupuncture like TENS and self-applied modes) after 8 weeks.

Conclusions: The RCTs discussed in this review suggest that acupuncture is an effective alternative treatment for improving the quality of life for patients diagnosed with endometriosis. However, it is inconclusive because some studies had a lack of a control group, small study size, failure to address previous treatment, and the number of sessions and the specific acupuncture sites necessary to obtain improvement in quality of life. It is necessary to address these issue in future studies.

Key Words: endometriosis, acupuncture, quality of life

## INTRODUCTION

Endometriosis is a condition in which endometrial tissue found inside the uterus grows outside of the uterus in areas of the body where it does not belong.<sup>3,6</sup> It causes a chronic inflammatory reaction where the blood is unable to escape, which then leads to the formation of scarring and adhesions.<sup>1,3,7</sup> Endometriosis affects 176 million women of all ethnic and social backgrounds worldwide and 1 out of 10 females in the US.<sup>8</sup> It is estimated that 10-15% of those women are of reproductive age while 40% are women suffering from infertility.<sup>1</sup> There is a delay in diagnosing endometriosis by several years because little is understood about the disease, causing it to be known as the “enigmatic disease”.<sup>1</sup>

Endometriosis can cause severe dysmenorrhea, deep dyspareunia, chronic pelvic pain, ovulation pain, cyclical or peri-menstrual symptoms with or without abnormal bleeding, infertility, and chronic fatigue.<sup>7</sup> The pain associated with endometriosis is described as crippling or likened to sitting on a needle.<sup>1</sup> It plays a big role in decreasing one’s quality of life. Many women are frequently absent from work or education opportunities which can affect their income and their ability to progress their income.<sup>1</sup> They may also have to cancel plans on short notice due to the pain they are experiencing and this can affect their social relationships in a negative manner.<sup>1</sup> Their relationship with their significant other is also affected because many women avoid sexual activity due to dyspareunia and the pain following intercourse that can last for hours.<sup>1</sup> There has been a significant improvement in understanding endometriosis; however, the pathology of endometriosis is still unclear.<sup>7</sup> It is thought that retrograde menstruation as well as immunological, inflammatory, genetic, and environmental factors play a key role.<sup>7</sup> Although retrograde menstruation is the most accepted theory, it cannot be the only factor because all

women experience some degree of retrograde menstruation but not all women experience the symptoms of endometriosis.<sup>1</sup>

Health care costs for endometriosis include direct health care cost, direct non-health care cost, and indirect costs.<sup>7</sup> It is estimated that \$22 billion is spent annually for endometriosis patients.<sup>7</sup> Annual healthcare costs and costs of productivity loss associated with endometriosis have been estimated at \$2801 and \$1023 per patient, respectively.<sup>7</sup> While women are awaiting a diagnosis, they are having a variety of interactions with healthcare providers and undergoing a variety of procedures to determine the cause for their symptoms.<sup>1</sup> There is no data showing the exact estimate of visits relating to endometriosis, but there were 23,194,000 visits for gynecologic conditions from 1995 to 1996.<sup>4</sup>

There is no cure for endometriosis, but there are medical, surgical, and pain management options that can help improve symptoms for patients with endometriosis.<sup>1,3</sup> Some current medical management options include GnRH agonists, synthetic androgens, oral contraceptives, injectable contraceptives, and aromatase inhibitors.<sup>3</sup> Some surgical management options include laparoscopic excision surgery, ablation, cauterization, and hysterectomy.<sup>1,2,6,8</sup> However, as with all treatment options, not all patients are candidates and each option will have a different effect on each patient. For example, GnRH agonists can cause menopausal symptoms and bone mineral loss that may be irreversible.<sup>1</sup> Although using contraceptives has been associated with some degree of success, it does prevent women from getting pregnant and some women are not at the point in their life where they wish to not become pregnant.<sup>1</sup> It has also been thought that having a total hysterectomy with bilateral salpingo-oophorectomy would cure endometriosis, but there are still women who have had this done that are dealing with endometriosis and its symptoms.<sup>1</sup> There has been a variety of research conducted to try and develop new treatment options.

Acupuncture is one of the newer treatment options that has been researched for patients to use as an alternative. It has been proposed that acupuncture improves symptoms associated with endometriosis which leads to a better quality of life.

## OBJECTIVE

The objective of this selective EBM review is to determine whether or not acupuncture is effective in improving the quality of life for women of reproductive age with endometriosis.

## METHODS

The studies discussed in this selective evidence based review included three randomized trials. The criteria used for the selection of these studies were based on specific populations, interventions, comparisons, outcomes measured, and type of study. The population included any female patient of reproductive age, greater than 18 years old with a confirmed diagnosis, and symptoms of endometriosis. The interventions used were acupuncture or acupuncture-like TENS (Transcutaneous Electrical Nerve Stimulation). TENS blocks the spinal cord and then releases opioids endogenously.<sup>6</sup> The first study compared the intervention group who received acupuncture to patients who received placebo point acupuncture after five sessions of acupuncture where 19 Dong Bang needles were inserted.<sup>2</sup> The second study compared the intervention group receiving acupuncture to a watch and see group.<sup>5</sup> However, after 3 months of watchful waiting the control group was able to participate in treatment.<sup>5</sup> The third and final study compared the intervention group receiving acupuncture-like TENS to a self-applied TENS group.<sup>6</sup>

All articles included in this study were randomized controlled trials, but one study was blinded while the other two were non-blinded. All were published in peer-reviewed journals from 2011 or later and were written in the English language. They were found on EBSCOhost,

PubMed, and Medline. The participants included in the first study had a diagnosis for endometriosis for at least 1 year, were 18-45 years old, had undergone a video laparoscopy, or had already undergone this procedure during the previous 3 years.<sup>2</sup> This study excluded participants that feared needles, used analgesics, had taken anti-inflammatory drugs in the 1 month before and during data collection, or had a pain less than 4.<sup>2</sup> The second study included participants that were 18-40 years old, had a history of histologically verified endometriosis and pelvic pain.<sup>5</sup> However, the study did exclude any participant that had undergone hormonal treatment during the month before enrollment, had a drug or alcohol addiction, was pregnant, had insufficient knowledge of German language, or had a contraindication for magnetic resonance imaging.<sup>5</sup> The third study included women at menopause, who were 18 to 50 years-old, who had been diagnosed with deep endometriosis in the cul-de-sac and/or intestinal loop, and who had hormone therapy  $\geq 3$  months with symptoms.<sup>6</sup> The study excluded participants that had decreased skin sensitivity, pacemaker, skin hypersensitivity, epilepsy, heart disease, or skin/bone abnormalities.<sup>6</sup>

Articles were selected based on their relevance to the clinical question and if they included patient oriented outcomes (POEMS). The key words used to find the articles for the selective EBM included the following: endometriosis, acupuncture, and quality of life. All the studies measured the effectiveness of acupuncture to improve the quality of life of women with endometriosis that had symptoms like chronic pelvic pain, dyspareunia, dyschezia, dysuria, and dysmenorrhea. The tools used for the measurements were the Endometriosis Health Profile 30 (EHP-30) and the physical and psychological sum score of the German version of the 12-Item Short-Form Health Survey. The significance of the outcomes was determined by using ANOVA p-value, Paired Wilcoxon test, paired t test, mean change, standard deviation and average. The

demographics and characteristics of inclusion regarding each study analyzed for the EBM is detailed below in Table 1.

**Table 1: Demographics & Characteristics of Included studies**

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
de Sousa <sup>2</sup> 2016	RCT, blinded	42	18-45	-Diagnosis for endometriosis for at least 1 year -Age: 18-45 years old -Undergoing a video laparoscopy or had already undergone this procedure during the previous 3 years.	-Fearing needles and using analgesics or anti-inflammatory drugs in the 1 month before and during data collection. -Pain less than 4	4	Five 40 minute sessions of acupuncture therapy (once per week)
Meissner <sup>5</sup> 2016	RCT, unblinded	67	18-40	-Age: 18-40 years old -History of histologically verified endometriosis and pelvic pain	-Hormonal treatment during the month before enrollment -Drug or alcohol addiction -Pregnancy -Insufficient knowledge of German language or CI for magnetic resonance imaging.	26	30-60 minute somatosensory stimulation from traditional Chinese medicine (acupuncture, moxibustion (heat) and cupping)
Mira <sup>6</sup> 2015	RCT non-blinded	22	18-50	-Women at menopause -Age: 18 to 50 years-old -Diagnosed with deep endometriosis in the cul-de-sac	-Decreased skin sensitivity -Pacemaker -Skin hypersensitivity -Epilepsy	0	Acupuncture like TENS

				and/or intestinal loop - Hormone therapy $\geq 3$ mos with symptoms	-Heart disease -Skin/bone abnormalities		
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OUTCOME MEASURED

The outcome measured in all 3 studies is improvement in quality of life for women with endometriosis upon completion of treatment. de Sousa TR et al (2016) looked at the quality of life before the beginning of the study and immediately after the intervention.<sup>2</sup> The outcomes were measured by using the Endometriosis Health Profile 30 (EHP-30), which is a self-reporting instrument that contains a core questionnaire consisting of 30 items assessing five dimensions.<sup>2</sup> The five dimensions included pain, control and impotence, emotional well-being, social support, and self-image.<sup>2</sup> Each scale was converted into a score from 0 to 100, with a lower score representing a better quality of life.<sup>2</sup> Mira T A et al (2015) used acupuncture-like TENS and self-applied TENS to determine the quality of life after 8 weeks of treatment.<sup>6</sup> Outcomes were measured like de Sousa TR et al by using the EHP-30 questionnaire.

Meissner K et al (2016) looked at the quality of life at baseline, at 3 months, and 6 months. The outcomes were measured by using the physical and psychological sum score of the German version of the 12-Item Short-Form Health Survey (SF-12). The SF-12 is scored so that a high score indicates better physical functioning. To calculate the Physical Component Summary (PCS) and the Mental Component Summary (MCS) scores, test items are scored and normalized in a complex algorithm. The PCS and MCS scores have a range of 0 to 100 and were designed to have a mean score of 50. Scores greater than 50 represent above average health status.

RESULTS

de Sousa TR et al (2016) used continuous data that was unable to be converted into dichotomous format. Originally, the study had a total of 46 participants with 23 women in the control group and 23 women in the experimental group and both groups contained participants with the same characteristics.<sup>2</sup> Only 42 patients were able to complete the study resulting in a 9.7% loss because 3 participants from the experimental group were excluded after finding a new job, becoming sick with cystitis and tonsillitis, early use of anti-inflammatories or analgesics, and 1 from the control group because of pregnancy (Table 1).<sup>2</sup> The experimental group and control group were characteristically similar. The experimental group received five 40 minute sessions of acupuncture that were done once a week where 19 Dong Bang Needles were inserted.<sup>2</sup> The needles were placed at specific acupuncture points like: Bilaterally at Bx 17, Vb 29, E36 for improving blood circulation in organisms, unilateral at VC3 for removal of adhesions caused by endometriosis, and bilateral at Bp 6, F3, F8, BP9, Bp10, R10 for regulating menstrual activity and female hormones and preventing new adhesions from forming and reflux of menstruation.<sup>2</sup> After 20 minutes, the needle withdrawal process began.<sup>2</sup> The control group went through the same process; however, the needles were inserted 3-cm apart from the original points and diagonally to the acupuncture meridian.<sup>2</sup> The data from the EHP 30 questionnaire was analyzed by applying repeated analysis of variance measures using the ANOVA p-value to calculate the statistical difference between the control group at the beginning of the study and immediately after the intervention. The quality of life before treatment was worse in Group 2 as opposed to Group 1 (p-value = 0.0008). However, the quality of life significantly improved after treatment in group 2. There was also a decrease in group 1, but it was not as significant of a decrease as compared to group 2. The SD value of the experimental group after treatment is 10.21. It is significantly large given that this study looks at that the responses to a questionnaire

on a scale from 0-100 and the lower the number the better quality of life. With such a high SD, it can cause the average score from the questionnaire to move into another category. Although there is a high SD, there is still a statistical improvement and it will have a positive effect on a bigger population. After interpreting the results and looking at the p-value, it can be confidently said that this is a statistically significant treatment. See table 2 for detailed results of this study.

**Table 2: Mean EHP 30 values and ANOVA p-value before the study and immediately after the intervention<sup>2</sup>**

	<i>Before Treatment</i>	<i>After treatment</i>
<b>Group 1 (control group)</b>	66.36±14.65 (n=23)	56.59±11.89 (n=22)
<b>Group 2 (experimental group)</b>	71.50±16.31 (n=23)	31.00±10.21 (n=20)
<b>Total</b>	68.81±15.49	44.40±16.97
<b>ANOVA p-value</b>	.0008	n/a

Just like the previous study, Meissner K et al (2016) also used continuous data. The control group was cared for by a gynecologist during their watchful waiting period and the intervention group was treated in an outpatient setting by a medical specialist for psychosomatic medicine and traditional Chinese medicine.<sup>5</sup> The treatment session for the intervention group was approximately 30-60 minutes.<sup>5</sup> The study began with 67 patients, but, before the intervention began, 4 participants were lost. Three participants were lost from the intervention group due to long distance and 1 participant from the control group due to pregnancy (Table 1).<sup>5</sup> After treatment was finished, the study lost 3 more participants, 1 participant from the intervention group due to psychiatric problems and 2 from the control group due to lost contact (Table 1).<sup>5</sup> The study also excluded patients from their data at the 6 month follow-up because 3 participants in the intervention group completed therapy before the 6 month follow-up and 8 participants from the control group began therapy after the 3<sup>rd</sup> visit.<sup>5</sup> Participants in both the treatment and control group were very similar in regards to demographics, diagnosis, and pain.<sup>5</sup> The data from the SF-12 questionnaire was analyzed by SPSS 23 and a p-value was obtained.<sup>5</sup> At baseline, the physical health sum score for quality of life was lower in the control group. At 3 months, there

was a significant mean change in the treatment but it was lower than the control group (p-value = 0.026).<sup>5</sup> There were 3 participants from the control group that did not return the questionnaire at the 3 month point, so their data was not incorporated into the study. However, at 6 months there was a significant mean change in the control group as compared to the control group (p-value = 0.446).<sup>5</sup> Again, there were participants who did not return their questionnaire, 7 participants from the intervention group and 1 participant from the control group. This mean change is relatively small. Therefore, it does not increase the average score from the pre-treatment by a large amount and at 6 months the mean change was bigger in the control group. However, there is still statistically significant evidence that there was improvement in the treatment group because the mean increased above 50. See table 3 for detailed results of this study.

**Table 3: Physical Health Sum Score (SF-12) at baseline with the Mean Change from baseline for Clinical Outcomes at 3 months and 6 months<sup>5</sup>**

	<i>Baseline</i>	<i>95% CI Mean Change at 3 months</i>	<i>95% CI Mean Change at 6 months</i>
<b>Treatment Group</b>	46.5±2.5 (n=34)	5.5±2.3 (n=32)	5.9±2.8 (n=21)
<b>Control Group</b>	42.2±2.6 (n=32)	1.7±2.4 (n=28)	7.4±2.9 (n=20)
<b>p value</b>	.020	.026	.446

The use of continuous data continued with Mira T A et al (2015). The study began with 22 participants (11 in each group).<sup>6</sup> There were no participants lost throughout the 8 week duration of the study.<sup>6</sup> The acupuncture-like TENS group consisted of 30 minute sessions once a week for 8 weeks where the TENS was applied to the S3-S4 with a frequency of 8 Hz and a pulse duration of 75  $\mu$ s and variation in intensity and frequency of 1 ms.<sup>6</sup> The self-applied TENS group applied the TENS twice daily at least 12 hours apart for 20 minutes.<sup>6</sup> They were placed at S3-S4 as well but with a frequency of 85 Hz and a pulse duration of 75  $\mu$ s.<sup>6</sup> Both groups allowed for the intensity to be adjusted to a point where it was comfortable but still strong enough to make a difference.<sup>6</sup> However, the self-applied TENS only had 3 adjustable options for intensity

that were 10, 20 and 30 milliamperes.<sup>6</sup> The data from the EHP-30 questionnaire was analyzed using the paired Wilcoxon test before and after treatment to obtain the p-value.<sup>6</sup> Before treatment, the acupuncture-like TENS revealed a statistically significant score much lower than the self-applied TENS (p-value = 0.002).<sup>6</sup> After treatment, both groups experienced a statistically significant decrease but the acupuncture-like TENS still had a lower score than the self-applied TENS (p-value = 0.01).<sup>6</sup> The average and SD for the acupuncture-like TENS post-treatment was 32.09±8.65. This SD value of 8.65 is large given that this study looks at that the responses to a questionnaire on a scale from 0-100 and the lower the number the better quality of life. Zero-30 signifies a high level quality of life, 31-60 being moderate quality of life, and 61-100 being low level quality of life. With such a high SD, it can cause the average answer to the questionnaire to move into another category. Despite this high SD, there remains a significant statistical evidence that shows that acupuncture-like TENS improved quality of life. However, a high SD reveals that this treatment will have a positive effect on a bigger population size. See table 4 for detailed results of this study.

**Table 4: EHP-30 average scores Pre and Post treatment<sup>6</sup>**

	<b>Acupuncture-like TENS (n=22)</b>	<b>Self-applied TENS (n=22)</b>
<b>Pre-treatment</b>	47.98±11.18	61.18±9.32
<b>Post-treatment</b>	32.09±8.65	46.88±13.91
<b>p value</b>	.002	.01

## DISCUSSION

Endometriosis is an underdiagnosed condition seen in the reproductive age of women worldwide. There is currently no cure for this disease and it commonly causes a variety of symptoms that leads to a poor quality of life. Therefore, it is important to determine an effective treatment to improve the quality of life for women with endometriosis. Since acupuncture has been known to be effective in the treatment of other gynecological disorders such as polycystic

ovary syndrome and dysmenorrhea, it is an adequate study to determine the effectiveness for the quality of life for women with endometriosis.<sup>2</sup>

Although the three studies discussed in this systemic review had no reports of negative side effects to acupuncture, they still have areas of concern. de Sousa TR et al (2016) used “placebo” acupuncture points which, like any other therapeutic intervention, can cause various outcomes and the actual effects at these points must be evaluated further.<sup>2</sup> Meissner K et al (2016) allowed both groups to take acute pain medication as needed during the study and they also allowed the control group to receive treatment after 3 months of watchful waiting and the interactions with a therapist could have had an effect on the results.<sup>5</sup> Mira T A et al (2015) used a small number of women to study, lack of a placebo, and the follow-up time was not a proper length.<sup>6</sup> Also, unlike the self-applied TENS, the acupuncture-like TENS allowed for interaction with a physical therapist during application which could have caused the greater improvement in quality of life.

## CONCLUSION

After review of the 3 RCTs, it is evident that they all demonstrated improvement in the quality of life for women of reproductive age diagnosed with endometriosis after acupuncture treatment. However, within some of the studies there was inconclusive evidence. For example, a control group was not always present during the entire duration of the study and the size of the study was not large enough. Some studies also failed to address if a person must have had previous treatment, the number of acupuncture sessions necessary to obtain improvement in quality of life, and the specific acupuncture sites. It is necessary to conduct further research to address these issues before stating that acupuncture is an effective treatment to improve quality of life for women of reproductive age diagnosed with endometriosis.

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