Effect of Low-Level Laser Therapy Versus Pulsed Electromagnetic Field on Cortisol Levels in Primary Dysmenorrhea: A Randomized Controlled Trial

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Abstract:

Purpose: to compare the effect of low level laser therapy (LLLT) versus pulsed electromagnetic field (PEMF) on cortisol levels in primary dysmenorrhea.

Methods: Forty females suffered from primary dysmenorrhea were distributed randomly and equally into 2 group (A) & (B); group (A) was treated with LLLT for 3 consecutive menstrual cycles, while group (B) was treated with PEMF for 3 consecutive menstrual cycles. The outcome measures, including serum levels of cortisol and scores of menstrual distress questionnaire (MDQ), were evaluated pre- and post-treatment.

Results: There were significant reductions in serum cortisol levels and menstrual distress questionnaire scores within the two groups (A) & (B) (p<0.05). Comparing between them post-treatment demonstrated that there was a significant decrease in serum cortisol levels in favour of group (B) (p<0.05), while there was a non-significant difference in MDQ scores between them post-treatment (p>0.05).

Conclusion: Both LLLT and PEMF are efficient modalities in management of primary dysmenorrhea, with a greater effect of PEMF on reducing serum cortisol levels.

Key words: Dysmenorrhea, low level laser therapy, pulsed electromagnetic field, serum cortisol, menstrual distress questionnaire.

1. Introduction

Primary dysmenorrhea is considered a pain during menstruation with exclusion of any pelvic disorders. It affects more than 50% of menstruating females (1). It has been suggested that increased levels of stress hormones, like cortisol, is associated with increased production of prostaglandins within the uterus, leading to excessive uterine contractility and subsequent uterine ischemia and hypoxia leading to primary dysmenorrhea (2,3).

Many females have a condition of exhaustion, so dysmenorrhea has a greater adverse effect on the normal activities of females, their work capacity, and employment of healthcare. It was correlated with increasing rates of work absences and limitation of daily activities. So, dysmenorrhea has the responsibility for financial fall contributed to the payment of medical drugs and health management as well as the reduced fertility (4).

Although analgesics, oral contraceptive pills and non-steroidal anti-inflammatory drugs (NSAIDs) are common treatments for primary dysmenorrhea, the failure percentage is between 20% to 25% because of their side effects and loss of effect in some women (5). Subsequently, alternative modalities for pain relief are desirable.

Since LLLT and PEMF have analgesic and anti-inflammatory effects, a previous study compared their effects on prostaglandin levels in primary dysmenorrhea. It found that both modalities are
effective methods in treating primary dysmenorrhea, with superior effects of PEMF (6). However, no study has been yet compared the effect of LLLT versus PEMF on cortisol levels, which act as an indicator for stress and increased pain intensity, in primary dysmenorrhea. Therefore, this study was the first one that aimed to compare the effect of LLLT versus PEMF on cortisol levels in primary dysmenorrhea.

2. Patients and Methods

2.1. Study Design

It was a prospective, randomized, controlled trial. Ethical approval was obtained by the Research Ethics Committee of the Faculty of Physical Therapy, Cairo university (No: P.T.REC/012/002321).

2.2. Participants

Forty females suffering from primary dysmenorrhea were chosen from the Gynecological Outpatient Clinic, Al-Mataria Teaching Hospital, Cairo, Egypt. All participants were chosen after diagnosed as primary dysmenorrhea. All of them were virgin with having a regular menstrual cycle (a menstrual duration of 3–8 days, with 21–35 days between each two successive menstrual cycles). The age was between 20-25 years old and the body mass index (BMI) of them extended between 18-25 Kg/m². The exclusion criteria were history of tumors, pelvic infection or inflammatory diseases, ovarian cysts, any gynecological disease, any hormonal abnormality and any psychological problem. Also, females having any contraindication for PEMF such as an implanted device like pacemaker, malignancies, neurological disorders with epilepsy and viral infections, as well as females having any contraindication for LLLT as malignant carcinoma, epilepsy, pacemaker and hemorrhage were excluded from the study.

2.3. Randomization

All females were instructed with a full explanation of the study protocol with signing a consent form before participating in the study, they were randomly and equally distributed into two groups (A) & (B) with the use of randomization cards generated by a computer. No subjects withdrew of the study after randomization.

2.4. Interventions

Group (A) included 20 females who received LLLT, 3 sessions every menstrual cycle, for 3 consecutive menstrual cycles, while group (B) included 20 females who received pulsed electromagnetic field (PEMF), 3 sessions every menstrual cycle, for 3 consecutive menstrual cycles.

2.4.1. Low level laser therapy (LLLT)

All females in group (A) received LLLT, 3 sessions every menstrual cycle, for 3 consecutive menstrual cycles. The 1st session was performed as the participant having intolerable pain (few hours or half a day before the beginning of the menstrual blood flow). Then, the 2nd and 3rd sessions were carried out in the next two consecutive days. The first female's position was supine lying for LLLT application on suprapubic region (6) with wave length between 808-905 nm, with frequency 1500 HZ and energy density of 4 J/cm² for 4 minutes. Laser was applied perpendicular on suprapubic region. Then, the female was asked to lie prone for the application of LLLT on the paravertebral region (L4-S3 ) (6), with wavelength between 808-905 nm, with frequency 1500 HZ and energy density of 4 J/cm² for 4 minutes. This process was repeated for 3 consecutive menstrual cycles.

2.4.2. Pulsed electromagnetic field (PEMF)

All females in group (B) received PEMF, 3 sessions every menstrual cycle, for 3 consecutive menstrual cycles. The 1st session was performed as the participant having of intolerable pain (few hours or half a day before the beginning of the menstrual blood flow). Then, the 2nd and 3rd sessions were carried out in the next two consecutive days. Before starting treatment session, each female in group (B) was instructed to evacuate her bladder to make sure that she was comfortable and relaxed throughout the treatment session. The female's position was a comfortable modified supine lying, with pillows and cushions supporting the body parts and sheets covering the female during sessions. Then, the PEMF electrodes were applied on the supra-pubic and the lumbo-sacral regions (L4-S3), and they were fixed by a long strap. The used parameters of pulsed electromagnetic field were 50 Hz in frequency, 60 Gauss in intensity and 30 minutes in duration (7). The treatment was repeated for 3 consecutive menstrual cycles.

2.5. Outcome measures

2.5.1. Serum cortisol level (primary outcome measure):

The blood samples were taken from each female in both groups to measure the serum cortisol levels, which could reflect the stress level and pain intensity as decreased cortisol levels mean decreased stress level and pain intensity. All blood samples were taken at 8-9 a.m., before and after the treatment. Samples were collected in prechilled test tubes containing EDTA and stored at -70ºC until analysis.
Analysis of serum cortisol levels were performed by radioimmunoassay, using Sigma-Aldich kits.

2.5.2. Menstrual distress questionnaire (MDQ) (secondary outcome measure):
It was used to evaluate the physical and psychological problems related to primary dysmenorrhea and influencing daily activities. It assessed 8 factors, covered by 47 items.

These factors included pain, concentration, behavioural change, autonomic reaction, water retention, negative effect, arousal and control. The participants were assessed through MDQ in both groups before and after treatment, through instructing participants to make (0) with non-symptoms, (1) with mild, (2) with moderate and (3) with severe symptoms (8).

Data analysis
Statistical analysis was established using SPSS version 19 for windows. Results were expressed as mean± standard deviation. The pre-treatment distribution of data was measured by test of normality, Kolmogorov-Smirnov test. Accordingly, unpaired t-test was performed to compare between normally distributed variables in both groups.

Analysis of covariance test (ANCOVA) was applied for comparing the post-treatment means of the two group on controlling the effect of pre-treatment value. Paired t-test was utilized for comparing within group (pre-treatment vs post-treatment) differences.

In not normally distributed data, Mann Whitney test was performed to compare variables in both groups. While test of Wilcoxon Sign Ranks was performed for comparison between pre- and post-treatment data in same group. P ≤ 0.05 was represented significant.

3. Results
At baseline, there were non-significant differences between both groups (p>0.05) in all variables (Tables 1-2).

The serum cortisol levels showed significant reduction within the two groups (A) & (B) with p<0.05. By comparing between groups after treatment, there were significant decrease in serum cortisol levels (p<0.05) in favor of group (B) (Table 2).

The MDQ scores showed significant reduction within the two group (A) & (B) with p<0.05. By comparing between groups after treatment, there were non-significant changes (p>0.05) (Table 2).

Table (1): Baseline data of females in both groups

<table>
<thead>
<tr>
<th>Group (A)</th>
<th>Group (B)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.45 ± 1.76</td>
<td>22.70 ± 1.75</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>60.35 ± 3.79</td>
<td>59.55 ± 3.50</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.50 ± 5.20</td>
<td>160.10 ± 3.75</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>23.73 ± 1.15</td>
<td>23.23 ± 1.13</td>
</tr>
</tbody>
</table>

NS P > 0.05 = non-significant, P = Probability.

Table (2): The serum cortisol level and MDQ scores for both groups

<table>
<thead>
<tr>
<th>Serum cortisol (µg/dl)</th>
<th>Group (A)</th>
<th>Group (B)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>28.39 ± 6.92</td>
<td>26.84 ± 6.60</td>
<td>0.473 NS</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>22.40 ± 6.78</td>
<td>17.38 ± 6.55</td>
<td>0.015 5</td>
</tr>
<tr>
<td>P value**</td>
<td>0.001 5</td>
<td>0.001 5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MDQ scores</th>
<th>Group (A)</th>
<th>Group (B)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>74.80 ±16.27</td>
<td>74.85 ±16.68</td>
<td>0.935 NS</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>51.05 ±16.80</td>
<td>48.80 ±15.88</td>
<td>0.534 NS</td>
</tr>
<tr>
<td>P value**</td>
<td>0.001 5</td>
<td>0.001 5</td>
<td></td>
</tr>
</tbody>
</table>

Data were expressed as mean ± standard deviation
Inter-group comparison; ** intra-group comparison of the results pre- and post-treatment.
NS P>0.05 = non-significant, 5 P<0.05 = significant, P = Probability

4. Discussion
Primary dysmenorrhea is a popular gynecologic problem which significantly influences women’s normal activity (9). The female with primary dysmenorrhea always suffers from psychological stress, which can disrupt the endocrine system leading to production of prostaglandins, myometrial contraction and dysmenorrhea (2). Therefore, this study was conducted to compare the effect of LLLT versus PEMF on cortisol, a stress related hormone, in primary dysmenorrhea.

Concerning serum cortisol levels, the findings of the current study indicated the positive effect of both LLLT and PEMF on reducing serum cortisol levels...
in females with primary dysmenorrhea, with a better effect of PEMF.

The significant reduction in serum cortisol levels within group (A) could be supported by Thabet et al. (10) who investigated that LLLT in addition to exercise for 3 months were effective in minimizing serum cortisol levels of dysmenorrheic females. LLLT has biological effects like that of NSAIDs. So, it can reduce pain through increasing production of serotonin that naturally enhances the mood of the body.

The significant decrease in serum cortisol levels within group (B) could be reinforced by Mortazavi et al. (11) who reported diminution of serum cortisol levels in response to electromagnetic field released from magnetostrictive cavitrons. Also, Pawluk (12) explained the valuable effect of PEMF on pain management through the reduction in cortisol and noradrenaline as well as the increase in serotonin, enkephalins and endorphins. Moreover, Strauch et al. (13) reported that PEMF acts like electro acupuncture; that by stimulation of painful tooth pulp in rats, the stress responses were decreased by electro acupuncture; also, norepinephrine, dopamine and cortisol all decreased.

The review of literature of this work was not detecting any study comparing the effect of LLLT versus PEMF on cortisol levels in primary dysmenorrhea. Therefore, the present study would be considered the first one concerning this point. Thus, the results of the present study could not be compared and discussed with other studies but revealed the significant better effect of PEMF over LLLT on reducing serum cortisol levels in primary dysmenorrhea.

Concerning MDQ scores, the findings of the current study reflected that both LLLT and PEMF have similar significant valuable effects on improving menstrual symptoms in females with primary dysmenorrhea.

Regarding the effect of LLLT on decreasing of dysmenorrheal pain, Mohamed (6) reported that LLLT is a non-invasive physical therapy modality that can reduce swelling, decrease pain sensation, treat acute injuries, and improve functional activity; LLLT is considered as a septic, anti-inflammatory, and analgesic modality, and it reduces pain through reducing inflammation and through its effect on serotonin metabolism by increasing 5 hydroxy indoleacetic acid in urine. Additionally, Shin et al. (14) used laser instead of needle for acupuncture in females experiencing primary dysmenorrhea.

Of the total 31 participants, they found that sixteen patients were satisfied in the 1st month, but five were satisfied in the 2nd cycle of LLLT treatment. Noteworthy, reduction of pain was stated by more than 80% of the participated females. Moreover, Thabet et al. (10) studied the effect of physical activity with LLLT on the pain during primary dysmenorrhea and concluded that pain intensity was reduced, with a complete pain relief in 76.67% of participants. The analgesic effect of LLLT is caused by different physiological mechanisms in the body through increasing production and release of endorphins, growth hormone, increased protein synthesis, venous and lymphatic flow, and increased angiogenesis.

In contrast, this study’s results disagreed with Kempf et al. (15) who used laser needle acupuncture. Although they have used different acupuncture points, visual analogue scale scores showed pain reduction, with no statistical significant changes. The contradiction of our findings with the findings of that previous study could be related to the difference in method and parameters of laser application, as well as the used methods for pain assessment.

Concerning the effect of PEMF on decreasing dysmenorrheal pain, the results of this study agreed with Abd El Aziz (7) who stated that magnetic field therapy has analgesic, anti-inflammatory, vasodilatation and anti-edematous activity without side effect and associated with an increase in pain threshold and anticoagulation system stimulation. It helps mast cells activation, opioid peptides production and increase of electric capacity of muscles’ fibers through direct effects which are firing of nerve ending, action potential of cell membrane, effect on release of endorphin, encephalin and dopamine, acupuncture actions and regeneration of nerves, and secondary effects on physiologic action were improving circulation, reducing swelling, increasing oxygen to the tissues, decreasing inflammation, promoting healing and altering prostaglandins levels.

The pain relieving effects of PEMF could be attributed to several mechanisms. The first mechanism involves the physiological mechanism for relieving pain through presynaptic inhibition or decreasing excitability of pain fibers. Second, the molecular mechanism may occur through changes in the ion channels or neuronal membrane. Third, the modulating effect of PEMF on the action of antibodies, hormones and neurotransmitters at receptors of different cell types. Fourth, PEMF reduces inflammation, improves circulation, and improves joint mobility by its effect on connective tissue, muscles and organs (16).

Moreover, PEMF improves production of interleukin-1 (anti-inflammation), reduces cytokines IL-1b (pro inflammation), resulting in inhibition of nociception (17). Furthermore, Hamza et al. (18) stated that PEMF might increase the release of...
nitrous oxide leading to boosting the analgesic effects in advanced inflammatory stage, and intensity of pain was reported to be oppositely correlated with nitrous oxide level.

These results were contradicted with that of Del Seppia et al. (19) who reported that PEMF has a high cellular biological stimulatory effect so it could be used with high precaution to the duration and the repeated number of its application. PEMF shouldn’t be applied for acute pain relief; however, it is most effective in treatment of chronic stage of pain through increasing pain stimulation and sensitivity leading to increase the endorphins and encephalin causing late pain relief.

Concerning similar valuable effects of both LLLT and PEMF on reducing menstrual symptoms in primary dysmenorrhea, this result was inconsistent with Mohamed (6) who reported better effects of PEMF than LLLT in reducing menstrual pain intensity, using present pain intensity, in females having primary dysmenorrhea. The contrast between our findings and the findings of that previous study could be related to the difference in treatment duration and the tools used for pain assessment.

The limitation of the current study is the lack of measuring the blood levels of different pain markers, so further studies are needed to measure the blood levels of different pain markers (e.g., serotonin, endorphin, neuropeptide Y, and substance P) to explore the mechanisms underlying the better effect of PEMF over LLLT on reducing serum cortisol levels in dysmenorrheal females. Also, additional research was recommended to assess the effects of various intensities of laser therapy on primary dysmenorrhea.

5. Conclusion
Both LLLT and PEMF are efficient modalities in management of primary dysmenorrhea, by reducing serum cortisol level and menstrual symptoms, with a greater effect of PEMF on reducing serum cortisol levels.

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Conflict of Interest
Authors declare no potential conflicts of interest.

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