Effect of Iontophoresis Treatment in Chronic Pelvic Inflammatory Disease

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ABSTRACT

This study was conducted to determine the effect of Dexamethasone Sodium Phosphate (DSP) iontophoresis in treating chronic pelvic inflammatory disease (PID). Thirty regularly menstruating patients diagnosed with chronic PID participated in this study selected from Outpatient clinic of Gynecology, Kasr Aini Hospital. They were treated with DSP iontophoresis for (8 mg/session). Each session was 40 minutes, three times / week for 12 weeks. All patients were evaluated before and after treatment using Present Pain Intensity (PPI) Scale as well as C- Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Count of White Blood Corpuscles (WBCs). The results of this study revealed high statistically significant decrease in PPI scores (P <0.001) as well as in CRP, ESR, WBCs after the end of treatment program. Accordingly, it could be concluded that DSP iontophoresis is an effective physical therapy modality alternative to drug given orally or by injection for treating chronic PID.

Keywords: Chronic pelvic inflammatory disease - Dexamethasone Sodium Phosphate iontophoresis - C- Reactive Protein - Erythrocyte Sedimentation Rate - White Blood Corpuscles.

INTRODUCTION

Pelvic inflammatory diseases (PID) is a clinical condition representing infection and inflammation of all or some pelvic organs. It is a common and morbid condition that affects 8-11% of women during their reproductive period. PID has high morbidity, about 20% of affected women become infertile, 20% develop chronic pelvic pain and 10% of those who conceive have an ectopic pregnancy.

The risk of infertility, ectopic pregnancy, and chronic pelvic pain is 5-10 times higher than in uninfected women. PID affects more than one million women between age of 15 and 35 years and generates annual health costs approximately 4.2 billion dollars where it is responsible for nearly 250,000 hospitalization per year. It was concluded that the risk factors of ovarian cancer including endometriosis and PID as both of them causes local pelvic inflammation that entails cell damage, oxidative stress and elevation of cytokins and prostaglandin, all of them may be mutagenic.

PID is a clinical spectrum of infection that may involve one or more of the following structures, the cervix (Cervicitis), the endometrium (Endometritis), the fallopian tubes (Salpingitis), the ovaries (Oophoritis), the uterine wall (Myometritis), broad ligaments (Parametritis) and the pelvic peritoneum (Peritonitis).

The most common clinical presentation of PID is bilateral lower abdominal pain and tenderness especially with walking and coitus, deep dyspareunia, abnormal vaginal discharge, chill and fever, less common symptoms include irregular vaginal bleeding, dysuria, nausea, and vomiting. PID may cause severe or minor symptoms, even with minor symptoms, it can cause damage to a
woman's reproductive organs. PID is most frequently assessed by clinical examination, measuring body temperature and determining serum leukocyte concentration and C-Reactive protein.

Opiates and non-steroidal anti-inflammatory agents are the mainstay of PID treatment that may reduce soft tissue inflammation. Pelvic surgeries have not been known to consistently relieve symptoms in patients with chronic PID, in some instances the situation was actually made worse by operative procedures.

Iontophoresis is a process that enhances the delivery of drug through a biological membrane via the application of low intensity electrical currents. This technology offers several advantages over oral and injection drug delivery. Key advantages of iontophoretic drug delivery include the avoidance of pain and the possibility for infection, inflammation and fibrosis associated with continuous needle injection. It reduces side effects of drug and permits its use with short biological half of life because the drug is delivered directly to the target organ. It eliminates gastrointestinal incomptability, enhances patient compliance with convenient and non invasive regimen.

Iontophoresis is becoming widespread today with many pharmacist compounding solution for this mode of administration. It has been called as a method of making needle less injection. It is non invasive, painless, sterile and tissue damage due to needle penetration is avoided. It has been successfully used to treat edema, inflammation and various skin conditions. In a recent study performed to compare which is more effective, safe and easy, the fentanyl iontophoresis or intravenous analgesia with morphine for controlling pain after major abdominal or orthopaedic surgery, it was concluded that fentanyl iontophoresis was more effective and safe as it enabled needle free, compact, self contained, self adhesive and it was applied to the patient's upper and outer arm or chest than intravenous injection.

Dexamethasone is an anti-inflammatory and analgesic drug, it inhibits cytokins in addition to inhibition of the migration for scavenger white blood cells to the site of inflammation. It stimulates the synthesis of enzymes required to decrease the inflammation response. Iontophoresis with DSP was effective in treating inflammation in several areas in the body. This study was performed to determine the effect of DSP iontophoresis in treating chronic pelvic inflammatory disease.

**SUBJECTS, MATERIALS AND METHODS**

**Subjects**

This study was carried out on thirty regular menstruating female patients were diagnosed with chronic PID and were selected from Outpatient Clinic of Gynecology department at Kasr Aini Hospital and their ages ranged from 25-35 years. All patients were free from diabetes, tubo-ovarian abscess, gynecological hemorrhage, pelvic tumors and spinal as well as sacroiliac joint pain. Also none of the patients was pregnant or using Intra uterine contraceptive device (IUCD) and they complained from lower abdominal pain radiating to the back with abnormal vaginal discharge as well as they were not responded to any previous medical treatment and were not taken any medication for pain and inflammation all through the study period. All patients were received (8mg/session) DSP iontophoresis for 40 minutes/session, three times per week for 12 weeks. The treatment was stopped during menstruation and continued after its stopping.
Informed consent form were signed by each subject before starting the treatment.

**Instrumentations**

**A- Evaluative instruments**

1- Pain Scales:
   a) Present Pain Intensity (PPI) Scale: It is a graphic rating scale with numerical values placed equidistantly along the line. The descriptors and numbers help the patient to place her estimate on the line (0-4)\(^1\).  
   b) Pain Relief (PR) Scale: it is similar to Present Pain Intensity (PPI) Scale.

![Pain Intensity Scale](image)

![Pain Relief Scale](image)

2- Ultrasound Machine: (Toshiba, 140 with vaginal Probe 7.5 MHz) was used to exclude any pelvic pathologic lesions.

**B- Treatment Instruments**

1- Iontophoresis (it is a light weight portable Iontophoresis device Inc. model 6110 PM in Houston, Texas, USA. It is a device provided direct current (0-5 mA) that connected with two disposable electrodes, one active and the other one is dispersive electrode\(^13,18\).

2- Plinth was used for application of iontophoresis.

3- Pillows were used to support cervical and lumbar curvatures of the patient to comfort and relax her during the treatment sessions.

4- Cotton and alcohol were used for cleaning the areas of electrodes applications.

5- Disposable syringes were used for injection of drug into the negative electrode and for drainage of venous blood samples to estimate CRP, ESR, and WBCs before starting as well as after the end of treatment program.
Procedures

A) Evaluative Procedures

1- Pelvic Ultrasonography: All patients were screened through Ultrasonographic examination to exclude any pelvic pathological diseases such as pelvic tumors, abscess and endometriosis before starting treatment\textsuperscript{13,18}.

2- Pain Evaluation: Assessment of pain intensity was done by using:

- Present Pain Intensity (PPI) Scale on which the pain intensity was scored by the patient as being: No pain = 0, mild pain = 1, moderate pain = 2, severe pain =3, and unbearable pain = 4 before and after treatment.

- Pain Relief (PR) Scale was scored by the patient as being: no relief = 0, slight relief = 1, good relief = 2, excellent relief = 3, and complete relief = 4, before and after the end of treatment.

3- Blood Sampling:

A sample of 5cm venous blood was drawn from anticubital vein for all patients by disposable sterile syringes before starting and after the end of treatment program to estimate C- Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR) and White blood Cells (WBCs)\textsuperscript{4,14,15}.

B) Treatment Procedures

Each patient was asked to evacuate her bladder before starting the treatment session to make sure that she was relaxed, then she was instructed briefly and clearly about the nature of iontophoresis and its values in treating pain and inflammation to gain her confidence and cooperation throughout the study. Each patient was asked to lie in a comfortable supine lying position on the plinth with small pillows under her head and lumbar region to accommodate her body curves\textsuperscript{8,9}. The basic principles for application for iontophoresis technique\textsuperscript{13,18} would be achieved by the following:

- The skin of the lower abdomen (supra pubic region) was prepared by cleaning it with alcohol to decrease skin resistance and decrease chance for skin irritation.

- The DSP drug (8mg) was injected in small chamber of the active electrode (Negative electrode)\textsuperscript{9,18}.

- The active electrode had a semi-permeable membrane which was self adhered to the patient skin that placed over the desired site of application with care to maintain a good contact between the skin and the electrode throughout the treatment session\textsuperscript{9}.

- The dispersive electrode (positive electrode) was placed at near site.

- The suggested distance between the delivery and the returning electrode was about the distance of one electrode.

The iontophoresis treatment session was started by low amplitude (1-2mA) for the initial period of treatment (10 minutes) then the current was increased for the reminder of the treatment session. The intensity was increased gradually till the patient reported feeling of tingling sensation if pain or burning sensation elicited the intensity was decreased. The treatment was given 3 session / week for 12 weeks (36 sessions) each session is 40 minutes\textsuperscript{10,11}.

Statistical analysis

Descriptive statistics was used for the collected data to calculate the mean, standard deviation, percentage and t-test for comparing between pre and post treatment measures. Significance level of 0.05 was used throughout all statistical tests within the study, P- value < 0.05 indicated a significant result. The smaller the P value obtained, the more significant was the result.
RESULTS

The results of this study revealed; before starting the study, the pain was felt unbearable in 10 cases (33.33 %), severe pain in 17 cases (56.67 %) and moderate pain in three cases (10 %). While, after the end of 36th treatment session, the pain was felt mild in 15 cases (50%), moderate pain in 1 case (3.33%) and 14 cases (46.67%) didn't feel any pain. There was a highly significant decrease (P < 0.001) of PPI scores when comparing mean values between before and after treatment (Table 1, Figure 1).

Table (1): Present Pain Intensity (PPI) scores before and after treatment.

<table>
<thead>
<tr>
<th>PPI Scores of PID Pain</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td>-</td>
<td>14</td>
</tr>
<tr>
<td>Mild Pain</td>
<td>-</td>
<td>15</td>
</tr>
<tr>
<td>Moderate Pain</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Severe Pain</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td>Unbearable Pain</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.23±0.59</td>
<td>0.56±0.40</td>
</tr>
<tr>
<td>% of change</td>
<td>81.12%</td>
<td></td>
</tr>
<tr>
<td>t-value</td>
<td>22.45</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>P&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

SD = standard deviation

Fig. (1): Mean values of PPI Scores before and after treatment.

There was a good relief of pain in 1 case (3.33 %), excellent relief in 15 cases (50 %) and complete relief of pain in 14 cases (46.67%). The mean value of pain relief was (3.43 ± 0.55) after the end of treatment (Table 2, Figure 2).

Table (2): Percentage of pain relief after the end of treatment.

<table>
<thead>
<tr>
<th>Pain relief Scores after treatment</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete relief</td>
<td>14</td>
<td>46.67</td>
</tr>
<tr>
<td>Excellent relief</td>
<td>15</td>
<td>50%</td>
</tr>
<tr>
<td>good relief</td>
<td>1</td>
<td>3.33%</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>3.43 ± 0.55</td>
</tr>
</tbody>
</table>

There were highly significant decrease in C-Reactive Protein, Erythrocyte Sedimentation Rate and count of White Blood Corpuscles (P < 0.001) when comparing between before and after treatment. (Table 3,4,5 and Figure 3,4,5).

**Table (3): Mean values of C-Reactive Protein before and after treatment.**

<table>
<thead>
<tr>
<th>C-Reactive Protein (mg/dl)</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>13 ± 4.76</td>
<td>5.03 ± 2.20</td>
</tr>
<tr>
<td>Mean difference</td>
<td></td>
<td>8.77</td>
</tr>
<tr>
<td>% of change</td>
<td></td>
<td>63.55 %</td>
</tr>
<tr>
<td>t-value</td>
<td></td>
<td>13.2</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

**Fig. (3): Mean values of C-Reactive Protein before and after treatment.**

<table>
<thead>
<tr>
<th>ESR mm / hour</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>26.27 ± 10.96</td>
<td>8.57 ± 3.70</td>
</tr>
<tr>
<td>t-value</td>
<td>15.56</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

PID is a major medical, economic and public health problem that affects about 8% of women during their reproductive period. Women with PID are more likely to have infertility, chronic pelvic pain, PID recurrence and ectopic pregnancy than women who haven't had the condition\textsuperscript{22,24}.

Iontophoresis is a non invasive technique used to deliver drugs across the skin for management of inflammation and pain\textsuperscript{19,28}. Thirty regular menstruating patients diagnosed with chronic PID, from Outpatient Clinic of Gynecology at Kasr Aini Hospital were participated in this study to determine the effect of DSP iontophoresis in the management of chronic PID\textsuperscript{17,20}. They received a treatment program of 40 minutes / session, 3 times / week for 12 weeks.

The results of this study showed a statistically highly significant decrease in pain intensity measured by PPI and PR Scales. The results agree with Grond et al. (2006)\textsuperscript{12} who reported that iontophoresis was an effective method for reducing postoperative pain after

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**Fig. (4): Mean values of ESR before and after treatment.**

**Table (5): Mean values of WBCs before and after treatment.**

<table>
<thead>
<tr>
<th>WBCs (10(^3)/mm(^3))</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>7.27 ± 1.77</td>
<td>6.72 ± 1.52</td>
</tr>
<tr>
<td>t-value</td>
<td>8.04</td>
<td></td>
</tr>
<tr>
<td>P- value</td>
<td>P &lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. (5): Mean values of WBCs before and after treatment.**
major abdominal or orthopaedic surgery. Also, Gokoglu et al. (2005) reported that surface application of iontophoresis over painful knee joints reduced perception of pain. These results indicate the potential effects of iontophoresis therapy as pain killer modality.

A statistically high significant decrease in pelvic inflammation measured by the levels of CRP, ESR and WBCs which come in agreement with Tikhonvskiaia et al. (2000) and Nevostruer et al. (2001) who reported that iontophoresis is an effective modality for treating inflammation either acute or chronic due to its inflammatory action. The results of the current study comes in agreement with Annese et al. (2005) as ESR, CRP and WBC were dropped although the period of the treatment was mismatched as his effect measured after one month and this study measurements were after three months.

Henderson et al. (2001) added that the analgesic effect of DSP iontophoresis therapy could be attributed to one of the following mechanisms, corticosteroids inhibit the inflammatory process, in part by reducing the migration of neutrophils and monocytes into the inflamed area and reducing the activity of these white blood cells. Corticosteroids have been shown to reduce "sprouting" that occurs in sensory nerves in association with tissue injury nerves. This "sprouting" may be one factor increasing the sensitivity of inflamed tissues to painful stimuli. However, Corticosteroids should not be applied to infected areas or to open wounds, because steroids tend to inhibit the immunologic defense process. The results of this study come in agreement with Howard et al. (2005) who stated that Dexamethasone is also given in this way to decrease inflammation. It works by acting within cells to prevent the release of certain chemicals that are important in the immune system. These chemicals are normally involved in producing immune and allergic responses, resulting in inflammation. By decreasing the release of these chemicals in a particular area, inflammation is reduced. This can help control a wide number of disease states, characterized by excessive inflammation. Nirschl et al. (2003) added that the experimentally induced inflammation and edema were significantly inhibited by exposure to DSP iontophoresis. As it was used to treat soft tissue inflammation by stimulating the synthesis of enzymes required to decrease the inflammatory response.

Accordingly, it could be concluded that DSP iontophoreses is an effective physical therapy modality alternative to drug given orally or by injection for treating chronic PID.

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الملخص العربي

تأثير التأين الكهربائي في علاج التهابات الحوض المزمنة

أجريت هذه الدراسة لمعرفة تأثير التأين الكهربائي باستخدام الديكساميثازون صوديوم فوسفات في علاج التهابات الحوض المزمنة لدى السيدات. وقد أجريت الدراسة على ثلاثين سيدة ذوات دورة شهرية منتظمة وتعانين من التهابات الحوض المزمنة وتم اختيارهن من العادة الخارجية لأمراض النساء. مستشفى قصر عين. وقد تم علاجهن باستخدام التأين الكهربائي بالديكساميثازون صوديوم فوسفات لمدة 40 دقيقة / الجلسة، 3 مرات أسبوعيا لمدة 12 أسبوع. وقد تم التقييم عن طريق مقياس شدة الألم، نسبة البروتين النشط سى، معدل سرعة الترسب في الدم، عدد كرات الدم البيضاء قبل وبعد الانتهاء من البرنامج. وقد أوضحت النتائج أن هناك انخفاض ذو دلالة إحصائية عالية في شدة الألم، البروتين النشط سى، معدل سرعة الترسب في الدم، عدد كرات الدم البيضاء بعد الانتهاء من البرنامج. وقد تم تخفيف درجة الألم، وذلك ينجم عن استخدام الديكساميثازون صوديوم فوسفات هو وسيلة علاج طبيعية فعالة وبدلة للعلاج الدوائي الذي يعاني بالغ أو عن طريق الحقن لعلاج حالات التهابات الحوض المزمنة لدى السيدات.