Provera Depot injection at the site of abdominal endometriosis; a comparative study

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Abstract:

Background: Endometriosis is a disorder of females in the reproductive age group, and it is defined as the presence of endometrial glands or stroma outside the uterine cavity. The usual location of presentation is usually the intrapelvic location and among them the ovarian form is the most frequent. Objective: To assess the most proper Provera Depot injection dosage and site in treatment of abdominal endometriosis. Patients and method: A prospective comparative study carried in private clinic in Baghdad city at the period from the 1st of July 2020 to the end of June 2021. The sample were included 30 women with cutaneous endometriosis diagnosed previously by ultrasound and divided into 3 groups. Results: significant decrease in pain in group treatment with intralesional 300 Depo-Provera than other groups (P=0.01), while no difference were found between the treatment groups regarding bleeding (P=0.7). mass size in intra muscular 150 mg Depo-Provera group was (2.3±0.8) cm before treatment and reduced to (2.2±0.9) cm after treatment, while the mass size in intralesional 150 mg Depo-Provera group was (2.7±1.01) cm before treatment and reduced to (2.1±1.4) cm after treatment, and the mass size in intralesional 300 mg Depo-Provera group was (2.7±0.3) cm before treatment and decreased to (1.5±0.6) cm after treatment. Conclusion: Treatment of abdominal wall endometriosis with intralesional 300 mg Depo-Provera were highly significant than other types of treatment.

Keyword: Depo-Provera, abdominal endometriosis, Intralesional injection.
Introduction:

Endometriosis is a disorder of females in the reproductive age group, and it is defined as the presence of endometrial glands or stroma outside the uterine cavity. The usual location of presentation is usually the intrapelvic location and among them the ovarian form is the most frequent. However, the extra-pelvic location can occur in more than 12% of women with endometriosis and affect any part of the body, including the skin [1]. Endometriosis usually presents as diffuse involvement, in plaques, although sometimes it does so adopt cystic or tumor morphology. When the endometriosis presents as a well-defined mass, it is called an endometrioma [2].

Cutaneous endometriosis is a disorder that primarily affects women of reproductive age and classically presents as a firm sub-cutaneous papule or nodule that averages 2 cm in diameter. Its color can range from blue or violaceous to brown or skin-colored. Patients frequently experience cyclical pain, swelling, and even bleeding that corresponds with their menstrual cycle [3].

To explain the pathogenesis of endometriosis, different theories have been postulated, including the theory of lymphatic or blood embolization, mechanical transport iatrogenic after abdominal or pelvic surgery, the theory of tubular regurgitation of the endometrium and the development of pluripotent cells of the coeloma, although most cases are not explicable by means of a single one of them, but through their joint application [1, 4]. The most typical form of presentation of primary cutaneous endometriosis is umbilical endometriosis, the incidence of which ranges from 0.5–1% of women with ectopia endometrial [5]. Primary cutaneous endometriosis has also been described in locations such as the perineum, joints or extremities, but these forms of presentation do not usually simulate tumors but are plaques or papules [6]. Most cases described cases of cutaneous endometriosis are secondary to surgery on the uterus or fallopian tubes, especially after abortion hysterotomies. The secondary form of post-caesarean section cutaneous endometriosis is very rare and its incidence ranges between 0.003 and 0.45% of cesarean deliveries [3, 6].

Cutaneous endometrioma symptoms are usually represented by a classic triad that includes the mass effect, pain, often cyclical and association with a previous surgical procedure. This characteristic clinical picture does not always appear, and so imaging tests such as ultrasound, magnetic resonance imaging and CT may be useful to reach the diagnosis. [7, 8].
Histologically, the endometriotic nodule is characterized by the presence of typical endometrial tissue made up of glands lined with columnar epithelium and stroma. The glandular epithelium can vary in response to hormonal changes, which translates clinically and histologically as hemorrhage or inflammation phenomena. The definitive diagnosis is histological, having to meet at least two of the following criteria: endometrial glands, stroma endometrial glands and / or hemosiderin deposits [9, 10].

Differential diagnosis with malignant endometriosis is based on the absence of cytological atypia and architectural proliferation. Although FNA can confirm the diagnosis of endometriosis and help to rule out the possibility of malignancy, it does not appear to be a conclusive test in the diagnosis and may also increase the risk of recurrence. Before the diagnosis of cutaneous endometriosis, the possibility of cutaneous endometriosis should be investigated. genital-pelvic endometriosis since the association with this can be up to 26% [1, 7-10]

Cutaneous endometriosis is very rare, so it is not usually taken into account in the differentiating diagnosis of subcutaneous tumors that affect the abdominal wall. Cutaneous endometrioma cases usually appear secondary to uterine surgery, are located in proximity to the resulting abdominal scar and the typical clinical manifestation is the mass and pain effect, often cyclical. Endometrioma of the abdominal wall is a pathology not referenced in the dermatological bibliography and when it appears it raises the differential diagnosis with other pathologies such as excessive fibrosis of the scars (gynecological surgery), an incisional hernia, a suture granuloma, an abscess, a traumatic neuroma, a hematoma, a desmoid tumor and rarely a soft tissue sarcoma or a metastatic carcinoma [11, 12].

Treatment:

The most effective treatment for cutaneous endometriosis is surgery. The endometriosis focuses between 5mm and 1 cm of adjacent healthy tissue should be included in the excision in order to avoid recurrence [3, 7-8]. The incidence of cancer in an endometriosis ovarian focus is 1%. The incidence of cancer in an extra pelvic endometriosis focus is unknown. Few cases of cancer have been described in abdominal wall endometriosis. It seems that frequent recurrence and the presence of atypical features in an endometriosis focus are two risk factors in the development of cancer on abdominal wall endometriosis. In some isolated studies, mutations in the PTEN gene (tumor suppressor gene with tyrosine phosphatase homology) have been found in up to 20% of
ovarian endometriotic cysts and in some of these cases they carry the PTEN gene mutation. The development of endometriotic ovarian tumors was observed. These mutations in the PTEN gene have not yet been demonstrated in other locations [1, 7, 13-15].

**Aim of the study:** To assess the most proper Provera Depot injection dosage and site in treatment of abdominal endometriosis.

**Patients and method:** A prospective comparative study carried in private clinic in Baghdad city at the period from the 1st of July 2020 to the end of June 2021. The sample were included 30 women with cutaneous endometriosis diagnosed previously by ultrasound and divided into 3 groups:

1. Group one: 10 patients were treated with IM 150 mg Depo-Provera (IM 150 mg DP)
2. Group two: 10 patients were treated with 150 mg Depo-Provera injected inside the lesion (Intralesional 150 mg DP)
3. Group three: 10 patients were treated with 300 mg Depo-Provera injected inside the lesion (Intralesional 300 mg DP)

**Statistical analysis**

SPSS version 26 (Statistical Package for the Social Sciences) used for entry and analysis of data. Results existing in the form of tables and graphs. Chi square test used to assess association between descriptive data and Fisher exact test used if the chi square test is not applicable. A one-way ANOVA is used for three or more groups of data, to gain information about the relationship between the dependent and independent variables. P value <0.05 will be considered significant.
Results: As shown in table 1 the mean age of the studied groups was (38.7±5.2) years with range between (22-51) years, with mean size of scar (2.8±1.02) cm. caesarean section was the most common surgical history (66.7%), the history of endometriosis was found in only (16.7%), the mass was found in scar in majorities of them and all mass were presented as single mass in the study.

Table 1: Patient demographic data and results of the study parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No.</th>
<th>%</th>
<th>Range</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>22-51</td>
<td>38.7±5.2</td>
</tr>
<tr>
<td>Size of scar (cm)</td>
<td></td>
<td></td>
<td>1-6</td>
<td>2.8±1.02</td>
</tr>
<tr>
<td>Previous surgical history</td>
<td>Cs</td>
<td>20</td>
<td>66.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gynecological surgery</td>
<td>4</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgical</td>
<td>4</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No history</td>
<td>2</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Endometriosis history</td>
<td>Yes</td>
<td>5</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>25</td>
<td>83.3</td>
<td></td>
</tr>
<tr>
<td>Location of mass</td>
<td>In scar</td>
<td>26</td>
<td>86.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outside scar</td>
<td>4</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>Number of masses</td>
<td>Single</td>
<td>30</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 show that there is significant decrease in pain in group treatment with intralesional 300 Depo-Provera than other groups (P=0.01), while no difference were found between the treatment groups regarding bleeding (P=0.7)

Table 2: Association between the treatment groups and the patient’s symptoms.

<table>
<thead>
<tr>
<th></th>
<th>IM 150 mg DP</th>
<th>IL 150 mg DP</th>
<th>IL 300 mg DP</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sever pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Absent</td>
<td>3</td>
<td>4</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Present</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Table 3, show that the mass size in intra muscular 150 mg Depo-Provera group was (2.3±0.8) cm before treatment and reduced to (2.2±0.9) cm after treatment with no significant difference found (P=0.7), while the mass size in intralesional 150 mg Depo-Provera group was (2.7±1.01) cm before treatment and reduced to (2.1±1.4) cm after treatment with no significant difference found (P=0.2), and the mass size in intralesional 300 mg Depo-Provera group was (2.7±0.3) cm before treatment and decreased to (1.5±0.6) cm after treatment with highly significant decrease found (<0.001)
Table 3: differences between cutaneous endometriosis mass size before and after treatment in the studied groups

<table>
<thead>
<tr>
<th></th>
<th>Abdominal mass size (cm)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>IM 150 mg DP (n=10)</td>
<td>2.3±0.8</td>
<td>2.2±0.9</td>
</tr>
<tr>
<td>IL 150 mg DP(n=10)</td>
<td>2.7±1.01</td>
<td>2.1±1.4</td>
</tr>
<tr>
<td>IL 300 mg DP(n=10)</td>
<td>2.7±0.3</td>
<td>1.5±0.6</td>
</tr>
</tbody>
</table>

Discussion:

Abdominal wall endometriosis is a rare form of presentation of endometriosis, described in 1886 by Villar and whose incidence is estimated to range between 0.5% and 1% of all patients with endometrial ectopy. Although in most cases it appears on surgical scars from abdominal or pelvic interventions in women of childbearing age, there are cases of spontaneous appearance [16,17].

The etiopathogenesis of cutaneous endometriosis and especially of the umbilical it is not clear, but various theories, not yet proven, have been postulated for the explanation of it. Examples of these theories are embolization of endometrial tissue by lymphatic or blood route that would explain spontaneous cases, metastatic implantation due to retrograde reflux after abdominal or pelvic surgery, the persistence of embryo-logical remnants of Mullerian tissue, tubular regurgitation and metaplasia of mesenchymal stem cells that transform into endometrial implants. However, most of the cases are not explained by a single of these theories, but require the joint application of several of them. The appetite of endometrial cells for scars is evident, for this reason the umbilicus would behave like a physiological scar for the settlement of said cells, which would explain the cases of spontaneous umbilical endometriosis. which is in agreement with that revealed in the current study when the majorities of mass were found in the scar (86.7%) [16-18].

Clinically it presents as a solitary nodule, exceptionally multiple, bluish, brownish or blackish in color and small in size, although it may increase and become painful in the premenstrual phase and produce secretions or bleeding during menstruation. The absence of these characteristic symptoms of endometriosis makes diagnosis difficult [1, 19].

In the present study significant decrease in pain in group treatment with intralesional 300 Depo-Provera than other groups (P=0.01), while no difference were found between the treatment groups regarding bleeding (P=0.7). Schlaff WD et al, found that Depo-Provera when injected intralesional
were reduced four of five endometriosis sign and symptoms after 6 months, while the effect of the medication after 18 months was reduced all these 5 symptoms of the disease [20]. Cheewadhanaraks S, et al, concluded that both postoperative Depo-Provera and postoperative oral contraceptive pills for 24 weeks were found to be effective and acceptable options for treating endometriosis-associated pain [21].

Moreover, current study shows that there is highly significant decrease in size of endometrial mass were found by treatment with intralesional 300mg Depo-Provera than other types of treatment (<0.001).

Conclusion:

Treatment of umbilical endometriosis with intralesional 300 mg Depo-Provera were highly significant than other types of treatment.

No conflicts of interest

Source of funding: self

Ethical clearance: was taken from the scientific committee of the Iraqi Ministry of health

References:


