Endometriosis- medroxiprogesterone versus triptorelinum

- clinical study -

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Abstract

Objective. *To assess which is better for the treatment of endometriosis diagnosed laparoscopically: medroxiprogesteron or triptorelinum?* ***Method.*** *The present study is a comparative study between two types of pharmacological treatment of endometriosis diagnosed laparoscopically, which could not be fully resolved surgically. Distribution is the following:*

- *first group of patients receiving medroxiprogesterone depot 150 mg/intramuscular once a month*
- *the second group receiving Triptorelinum 3.75 mg/intramuscular every 4 weeks After 6 months of drug treatment, patients in the two groups are subjected to second-look laparoscopic surgery to be able to compare the effectiveness of two types of medication.* ***Results.*** *The study is still in progress because we are still enrolling patients. Until now we have completed the evaluation of 13 women (five received medroxiprogesteron and eight received triptorelinum). At the second look laparoscopy we found that 7 out of 8 patients from the triptorelinum group had a degree of endometriosis recurrence and three out of the five patients who tolerated medroxiprogesteron had no endometriosis recurrence.* ***Conclusion.*** *In these particular cases we were able to observe that for our patients medroxiprogesteron is more poorly tolerated than triptorelinum but with better results regarding endometriosis recurrence and symptomatology.*

Keywords: *endometriosis, medroxiprogesteron, triptorelinum*

Introduction

To assess which is better for the treatment of endometriosis diagnosed laparoscopically: medroxiprogesteron or triptorelinum?

Endometrial cells implanted ectopically respond to cyclical changes in estrogen and progesterone with proliferation and secretion. Their presence in extrauterine areas can initiate immune and inflammatory responses that lead to pain and peritoneal adhesions, and may interfere with fertility[(1)].

The most frequent clinical presentations of endometriosis include dysmenorrhea, chronic pelvic pain, dyspareunia, infertility, pelvic mass, urinary problems, pain related to bowel movements and ovarian endometriomas. Endometriosis has no cure but the symptoms can be managed well in most cases[(2)].

However, the correlation between these symptoms and the stage of endometriosis is poor. Diagnosis is based on the occurrence of cyclical symptoms and surgical validation via laparoscopy or laparotomy.

Endometriosis seems to regress when the ovaries are inactive; therefore, therapy that suppresses the ovaries is generally recommended. Oral contraceptives (OCs), progesterone preparations, androgens, and gonadotropin-releasing hormone agonists alone or in combination with nonsteroidal anti-inflammatory agents are all effective in reducing the severity of the symptoms. The alternative to medical therapy is surgery. Typically surgery is combined with postoperative medical therapy to delay disease and symptom recurrence[(3)].

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Methods

Study design

The present study is a comparative study between two types of pharmacological treatment of endometriosis diagnosed laparoscopically, which could not be fully resolved surgically.

It has the approval of the Ethics Committee from the Hospital of Obstetrics and Gynecology "Prof.Dr. Panait Sarbu" Bucharest.

Distribution is the following:

- first group of patients receiving medroxyprogesterone depot 150mg/intramuscular once a moth)
- the second group receiving Triptorelinum 3.75 mg intramuscular every 4 weeks.

After 6 months of drug treatment, patients in the

two groups were subject to second-look laparoscopic surgery to be able to compare the effectiveness of two types of medication. Were analyzed and compared patients with severe endometriosis and similar in location and degree of damage.

Evaluation and treatment is according to current guidelines and recommendations, therefore we use the American Society for Reproductive Medicine classification - each patient will have a certain score. Depending on the staging, patients are randomly divided into two groups (it will compare the predominant involvement of a particular anatomical sites, age, degree of fertility - the number of births or abortions prior to the study). We are interested that the two final groups to be similar in distribution depending on the degree of impairment of endometriosis, its location and age.

Study population

The proposed project aims mainly the detection of women affected by endometriosis (clinical symptoms - infertility, ultrasound, MRI and laparoscopy) and attempt to resolve it surgically (depending on location).

Patients are enrolled as they present at the hospital for various complaints related to endometriosis, are well informed regarding the pathology, treatment possibilities and its limitations. History, physical examination and laboratory findings determine which patients can enter or not in trial, considering the side effects of drugs. According to the results we have:

- **Inclusion criteria:** laparoscopically diagnosed endometriosis, non-pregnant state, aged between 18 and 45 years, absence of associated pathologies that make medication impossible.
- **Exclusion criteria:** state of pregnancy, other conditions that require immediate treatment (cervical pathology etc.), conditions that contraindicate treatment (thrombosis, coagulopathy, cardiovascular disease, cerebrovascular disease, cholestasis or symptomatic gallstones, neoplasia, liver tumors (benign or malignant), undiagnosed abnormal uterine bleeding.

At the first (admission) the patient sign the informed consent to enter the program.

All patients are examined clinically at study entry, recording the following data sheet:

Detailed medical history that these data were obtained:

- menarche, last menstrual period, previous hospitalization tasks
- complete history of the disease endometriosis: the age at which disease was diagnosed, clinical manifestations of onset, investigations conducted, including previously conducted laboratory balance in study, performed surgeries and treatments.
- family history, family history of endometriosis prevailed

Clinical examination of each patient, when including them in the trial, is complete and includes:

- general clinical examination equipment and systems (measurement in standardized conditions of BP, pulse and BMI)
- breast examination
- gynecological examination (including colposcopic exam and Pap test)
- laboratory tests: CBC, glucose, urea, creatinine, uric acid, transaminases, coagulation, urinalysis exam
- patients will appreciate the pain using visual analog scale from 1 to 10
- each patient will receive a questionnaire/schedule where she have to note the evolution of symptoms after starting treatment
- patients will note what other medications are used to improve comfort and quality of life, and satisfaction regarding treatment.

Data for the study. A unified study sheet for all patients include all data above. All data is beeing transferred into a unified database for the purpose of subsequent statistical analysis.

The two groups are comparable regarding grade of endometriosis, location and age but not all patients are matched due to the small number of cases. Age varied between 28-39 years old. Location of endometriosis: ovarian, peritoneal, intestinal. Degree of endometriosis: stage III (16-40 points).

Results

We have 13 patients who finished their complete evaluation. Eight of them received triptorelinum (group number 1) and the other five received medroxiprogesteron (group number 2). The two groups were matched in regards of degree of endometriosis (stage III) and age. All of the patients had ovarian endometriosis (one or both ovaries) and extensive adherents. One patient had intestinal endometriosis and it is a part of the first group.

During the first laparoscopy all ovarian cysts were surgically removed (cystectomy) and adhesion were partially or totally dissected. Between 50 to 70 percent of peritoneal endometriosis was electro coagulated.

In the first group, there were 7 patients had bilateral ovarian endometriosis cysts and adhesions and one had an ovarian cyst and adhesions. In the second group (medroxiprogesterone), all the patient had bilateral cystic endometriosis and adhesions.

After six moth of treatment the "second look" laparoscopy revealed the following:

Endometrial recurrence:

Group 1: All of the patients with bilateral cysts which were removed during the first laparoscopy had a recurrence of endometriosis cyst on one ovary representing about 60% of the volume of one of the initial cyst (only in one case we found adhesions, a serous cyst and small ovarian outbreak of endometriosis after a bilateral cyst).

Group 2: In all three cases that tolerated the treatment at the second look laparoscopy there were no more endometriosis cyst present.

Adhesions:

The adhesions were fairly the same between the two laparoscopies in both groups.

Side effects:

During the six moth of treatment they filled out their questionnaire regarding the symptoms and medication side effects.

They graded the severity of symptoms in a scale from 1 (minimum) to 10 (maximum).

Group 1: hot flushes, migraine, "bone pain".

All of them described hot flushes grading them from 7 to 8.Two patients had migraines which were considered the worst (grade 9 - symptom that had never appeared before triptorelinium administration).

"Bone" pain was described by 5 of 8 patients and the severity was between 5 to 6.

Group 2: heavy bleeding, neurological disorder.

During the six month of treatment 2 of the 5 patients stopped the medroxiprogesteron administration due to heavy bleeding in one case (after two months of treatment the bleeding started. Ultrasound showed thick endometrium of 16 mm and a curettage was necessary to stop the bleeding. The histopathological exam showed an intense progesterone reaction of the endometrium) and neurological disorder in another case (lipotimias - started after the administration of treatment and ended when the administration stopped).

Limitation of the study: small number of cases with no statistical relevance, uneven number of cases (not completely matched).

Conclusions

In these particular cases we were able to observe that for our patients medroxiprogesteron is more poorly tolerated than triptorelinium but with better results regarding endometriosis recurrence and symptomatology. Once our study is growing will have more statistical significance. ■

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