

PREVENTION WITH DESORGESTREL OF ENDOMETRIOUS CYSTS RECURRENCE AFTER SURGICAL TREATMENT

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Abstract. Currently, endometriosis is an important public health issue due to the increasing number of cases and the risk of developing ovarian and endometrial tumours (10% of ovarian endometrial carcinomas are associated with uterine endometrioid carcinomas), which has led to increased research into the mechanisms of appearance and progression of this condition. Although endometriosis is considered a benign chronic disease, it can show an invasive character causing severe symptoms. Endometriosis has an increasing incidence, affecting 2% of the general population, being the third gynecological cause of infertility, chronic pelvic pain, dyspareunia and dysmenorrhea. Endometriosis affects 7-15% of women of childbearing age, with 25-30% of sterility cases having a significant social impact. Endometriomas are difficult to excise due to vascularization and increased adhesion of the cyst wall. Surgical treatment of endometriosis is effective in the short term. Surgery most often reduces ovarian reserve. The rate of recurrence after surgery can be reduced with the help of menstrual suppression medications such as hormonal contraceptives. Desogestrel treatment improves intraoperative conditions mainly by reducing bleeding and increasing laxity between cyst coat and normal ovarian tissue.

INTRODUCTION

Until now, the etiology of endometriosis remains unknown, although several theories have been issued and have attempted to explain this inflammatory disease. Retrograde menstruation is the most accepted theory (Bulun, S.E., 2009; Aznaurova, Y.B., et al, 2014).

Endometriosis is a relatively frequent gynecological disease, usually characterized by infertility or chronic pelvic pain. In the ovary, most commonly, endometriosis is manifested by the appearance of endometriomas, those cysts containing a chocolate-like substance and a pseudocapsula that is adjacent to normal ovarian tissue, adherent to peritoneum, fallopian tubes and intestine (Giudice, L.C., 2010; Verkauf, B.S., 1987).

This disease can be confirmed only following surgery, usually laparoscopic. Endometriomas are in particular difficult to remove because the surgery can reduce the ovarian reserve, the capsule being very adherent and well vascularized. Surgical resection of endometriotic implants is often associated with partial disappearance of symptoms or their relapse, therefore prolonged medical treatment may be necessary (Lucidi, R.S., et al, 2005; Vercellini, P, et al, 2011).

Surgical treatment of endometriosis is effective in the short term, but if the patient does not get pregnant shortly after surgery, the recurrence is common. The rate of recurrence after surgery may decrease with the use of menstrual suppression treatment consisting of the administration of hormonal contraceptives. Desogestrel is a progestogen derived from 19-nortestosterone, widely used for oral contraception, both in combination with ethinylestradiol and plain, in mini-pill contraceptives (Peltecu, Gh., 2014).

Endometriosis appears to be a complex disorder in which a variety of factors (environmental, hormonal, immune and genetic) are involved, being considered a hormone-addictive disorder (Bedaiwy, M.A. & Falcone, T., 2004).

Many studies have proved that desogestrel has superior properties than other progestative pills in the preoperative treatment of endometriotic lesions and that is why we studied its effects when treatment was continued postoperatively by the patients who had undergone surgery for removing their endometriotic cysts (Wu, M.Y. & Chauk, H; 1996; Foda, A.A, et al, 2012).

The quality of life correlated with health is a multidimensional concept that involves physical, psychological and social aspects associated with the disease and its treatment (Bedaiwy, M.A., et al, 2002).

The purpose of the study. This study sought to evaluate the effects of continuous treatment with desogestrel versus oral contraceptives combined (0.02 mg ethinylestradiol/3 mg drospirenone) in the prevention of postoperative recurrence of endometriotic ovarian cysts.

MATERIAL AND METHOD

Our study included 300 patients with endometriotic ovarian cysts that undergone surgery at “Elena Doamna” Clinical Hospital of Obstetrics and Gynecology in Iași, in the period of time 2010 – 2017. The cysts were diagnosed during pelvic examination or transvaginal ultrasound performed for infertility, chronic pelvic pain, abnormal vaginal bleeding or during a routine control (fig. 1). The minimum diameter of a cyst was 20 mm, and patients with septal cysts, papillomas or peritoneal fluid were excluded from the study.



Fig. 1. Ultrasound changes preoperatively (personal collection)

We also excluded from the study women with a body mass index > 30, with neoplasms, autoimmune diseases, diabetes mellitus, infectious diseases, developing pregnancy or under anti-inflammatory or hormonal treatment. Every patient enrolled in the study signed the consent form.

The patients were divided into 3 batches, 100 of the patients followed treatment with desogestrel (Cerazette) 75 mg, 100 of the patients were treated with combined oral contraceptives (0,02 mg ethinylestradiol/3mg drospirenone), and 100 patients did not follow any treatment, as they refused treatment because they wanted to undergo surgery and conceive immediately after it. The duration of treatment was 6 months before laparoscopy and another 3-6 months after surgery.

During the surgery, we evaluated the cyst size, vascularization, uterine and contralateral ovary position, presence of adhesions, and ease of dissection of cyst coat from normal ovarian tissue. All cases were confirmed by a pathological examination that highlighted histological aspects of endometriosis: endometrial stroma, endometrial epithelium, glands responsive to hormone stimuli and hemosiderin deposits.

Intraoperatively there was less bleeding when removing the cyst coating, which suggests a better cleavage plane between the cyst coating and the normal ovarian tissue.

Desogestrel treatment was well tolerated and no patient gave up the study due to adverse effects (tab. I).

Table I. Tolerance of Desogestrel treatment

	Desogestrel	COC
Cleavage plane	+++	+/-
Bleeding	+/-	+++
Adhesions	+	+++
Duration of intervention	+	++

Patients were monitored by Doppler endovaginal ultrasound every three months. The Characteristics of the two treatment groups were compared using Student’s *t*- and χ^2 -tests.

The patients were aged between 18 and 45 (the mean age being of 34 years old), all still having menstruation. 206 of the patients had infertility associated with endometriosis.

RESULTS AND DISCUSSIONS

The mean age was significantly higher in the group of patients receiving COC (28.98 vs 39.24 y; $p=0.05$).

Preoperative, it was found by ultrasonograph that in over 80% of the patients treated with desogestrel vasculature was decreasing ($p=0.039$) (fig. 2).

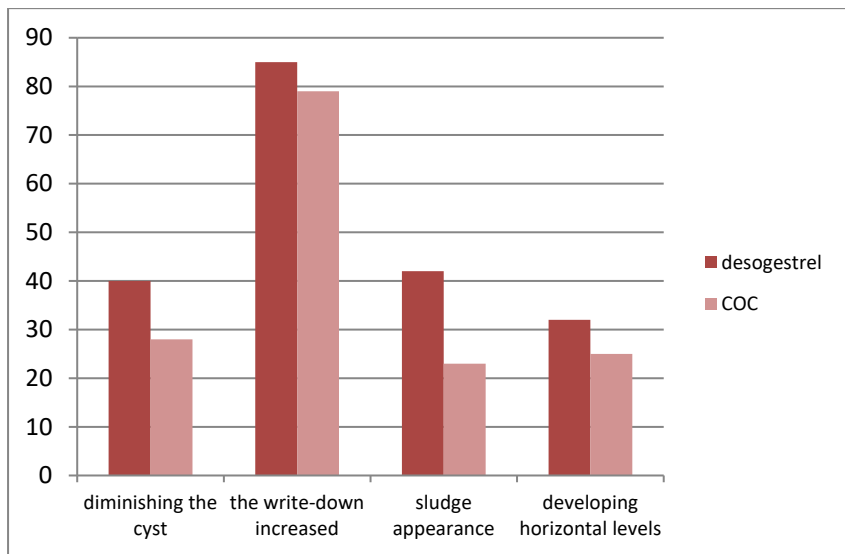


Fig. 2. Preoperative ultrasound changes

For the group treated with desogestrel, 80% of patients had amenorrhea, 58% had irregular bleeding and 17% of the women accused regular bleeding. Patients described these bleeds as being much less quantitatively than normal menstruation. 51% of the patients accused a weight gain of a maximum 5 kg, 28% of the women reported vaginal dryness and sexual discomfort, and 55% of the patients reported a decrease in libido (fig. 3).

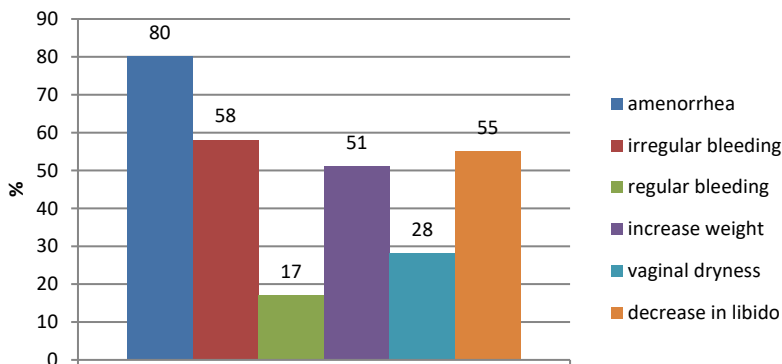


Fig. 3. Side effects in treated group

Patients treated with combined oral contraceptives did not have the adverse effects of desogestrel except for weight gain in a similar proportion, but instead 80% of the patients accused breast-stress, 10% headache, 7% nausea; symptomatology has improved from one month to the next. Therefore, both batches tolerated treatment well and no patient gave up the study due to adverse effects.

In the group with desogestrel, 70% of the patients were pregnant in the first year after laparoscopy, in the group who received oral contraceptives 67% were pregnant and in the non-treated group 63% of the patients conceived in the first year postoperatively. The cyst recurrence rate was significantly lower (6%) in the group of patients receiving desogestrel, respectively 7% in group 2 compared to the group of patients who did not receive any treatment (fig. 4).

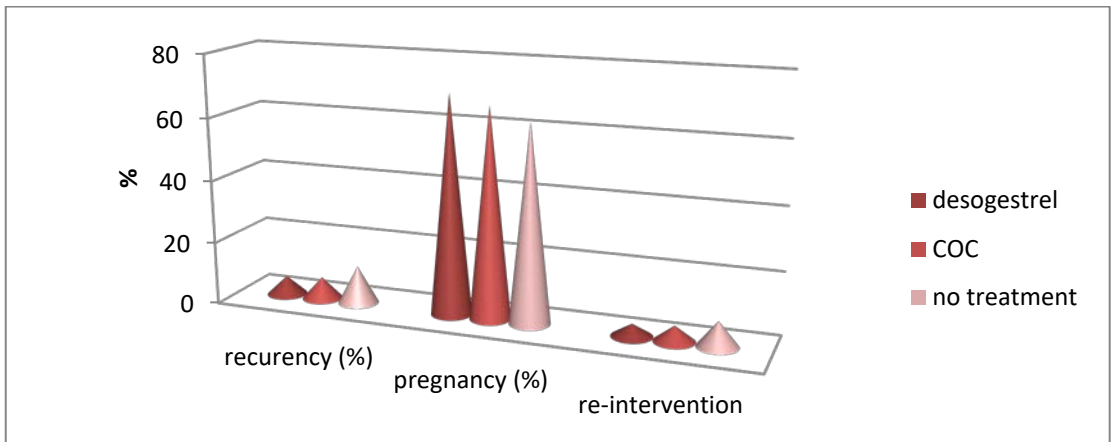


Fig. 4. Patient monitoring in the first postoperative year

According to the American Society for Reproductive Medicine, "Endometriosis should be considered a chronic illness that requires a life-long management plan to maximize the use of medication and avoid repeated surgical procedures" (Johnson, N.P. &Hummelshoj, L., 2013).

Hormonal drugs are given to try to stop ovulation for as long as possible in order to keep the implants or lesions from being aggravated. These can include oral contraceptives, progesterone drugs, and GnRH agonists (Barbieri, R.L., et al, 1986; Pittaway, D.E. & Douglas, L.W., 1989; Koyama, N, et al, 1993). Most of these therapies can only be given for a limited amount of time, and the side effects can cause problems for some women. Hormonal drug therapy is used to ward off symptoms and is often most effective when used after surgical treatment has been done (May, K.E., et al, 2010).

Endometriosis can cause infertility in many women, but with proactive treatment, the possibility of pregnancy is increased (Burney, R.O. & Giudice, L.C., 2012; Streuli, I., et al, 2013).

CONCLUSIONS

Drug treatment should contribute to two main objectives: reducing pain for prolonged periods and preventing the aggravation of the disease between the conservative surgery and the moment of conception.

Progesterone treatment optimizes intraoperative conditions and reduces the risk of recurrence of endometriosis.

Continuous treatment with desogestrel prevents recurrence of endometrial cysts and clinical symptoms related to endometriosis. Desogestrel offers the associated benefits of a well-tolerated contraceptive and allows for a safe postponement of the planning of a child without the risk of a relapse of the disease.

The treatment has a low cost, is effective and brings a considerable improvement in the quality of life of the patients.

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