

## Teenage and Postmenopausal Endometriosis

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### Introduction

Endometriosis is a chronic inflammatory disease resulting from the growth of endometrium outside the uterine cavity. The disease could affect various parts of the body including the pelvic cavity, the abdominal organs, the lungs and the pleura and scars of previous abdominal surgery. So, the disease is not limited to the pelvic cavity. Furthermore, endometriosis has been reported in the teenage population and also in postmenopausal women.

### Endometriosis in Teenagers

Recently, many data appeared in the literature indicating that endometriosis can occur in teenage girls [1]. In the past the occurrence of pain in teenagers was considered as a normal phenomenon related to the occurrence of menses. However, the pain has been present all the time, also intensifies during menses. It has been described as gastrointestinal, muscular activity or dysmenorrhea. With the evaluation of this pain, using ultrasounds, other radiological methods and also laparoscopy, it has been found that this pain in the majority of cases is due to endometriosis [2]. The diagnosis of endometriosis in teenagers has been delayed for years. Now as we know that endometriosis can occur in adolescent girls, the evaluation as early as possible, will confirm the disease and the teenagers will be able to function easy with proper treatment [3].

### Postmenopausal Endometriosis

Endometriosis is a disease that needs estrogen for the cells to grow. In menopause, estrogen levels are very low since the ovaries are not functioning. It was first reported in 1950. However, cases of postmenopausal endometriosis have been reported in 2-5% [4]. As was discussed before in the pathogenesis of endometriosis, local estrogen production is produced from the stroma of these cells. This is due to the action of aromatase P450,

that converts testosterone to estradiol and androstenedione to estrone. Thus, endometriosis will continue its growth and will lead to symptomatology, essentially pain [5].

Postmenopausal patients complaining of pain, must consider endometriosis in the differential diagnosis. In order to verify this, the patient will go through the investigational process including ultrasound and MRI. The final diagnosis will be through laparoscopy to check the lesions, confirming the diagnosis using biopsy and also excising the lesions or using cautery or Co2 laser.

If medical treatment is used then aromatase inhibitor will be the ideal and effective treatment for these patients. Unopposed estrogen, progesterone, GnRH and danazol are ineffective in treating postmenopausal endometriosis. Furthermore, unopposed estrogen treatment may increase chances of malignant changes in these endometrial implants.

### Aromatase P450 Effect in Endometriosis

Aromatase is an enzyme that is found in the endometrium of endometriosis patients. It is not present in the normal endometrium. This is one of the factors that keep the endometriosis cells functioning and recurring after treatment. This is due to the fact that aromatase converts testosterone to estradiol and converts androstenedione to estrone. The available lines of treatment of endometriosis as birth control pills, progestins and Danazol act on the hypothalamic pituitary axis and inhibits estrogen production by the ovaries. This does not affect estrogen production by aromatase. The end result is recurrence of endometriosis [5-7].

### Use of Aromatase Inhibitors in Treatment of Endometriosis

Endometriosis was estimated to affect 176 million women in the world in 2010. Medical treatment that has been in use for this disease includes contraceptive pills,

Danazol, Medroxyprogesterone acetate and gonadotropin releasing hormone agonist.

Aromatase inhibitors act on endometrial aromatase thus decreasing estrogen synthesis from endometrial cells and stroma. This will be great for postmenopausal endometriosis since the estrogen source is the endometrium and fatty tissue in various parts of the body. The situation is different in young patients who still have a functioning ovary. Therefore, treatment of these patients requires the addition of another line of treatment to take care of the other estrogen sources and thus the treatment will be effective.

There are 3 generations of aromatase inhibitors. The first generation are administered intramuscularly and they induce medical adrenalectomy. The second generation are also administered intramuscularly and they are associated with less side effects. The third generation are administered orally. They decrease serum estradiol by 97-99% within the first 24 hours after administration.

The use of aromatase inhibitors with gestagens or GNRH agonist, have demonstrated reduction of pain and also the size of the lesions of endometriosis. This was evident in 10 clinical studies totaling 137 patients (Nawathe et al.) [8] and another clinical study by Ferrero et al. [9] with a total of 251 patients. The European Society of Human Reproduction and Embryology recommend the use of aromatase inhibitors with oral contraceptives or progestogens or GNRH agonist in patients with drug resistant or surgery resistant rectovaginal endometriosis.

Aromatase inhibitors are effective for treatment of postmenopausal endometriosis. Endometriosis incidence is 2-5 percent of the postmenopausal women. Aromatase inhibitors were shown to reduce the pain and also the size of the endometriosis lesions. The main source of estrogens postmenopausally is extra ovarian. One of the issues in treating postmenopausal women is the hypoestrogenic status that will lead to osteopenia and osteoporosis. Bone density study is to be considered as a follow up of treatment of these patients [10].

### **Effect on Bone Metabolism During Aromatase Inhibitor Treatment [11,12]**

Long term treatment of endometriosis using aromatase inhibitors showed decrease in bone mineral density, but no patient developed osteopenia or osteoporosis. The American Society of Clinical Oncologists recommend testing for bone mineral density once per year for those patients on aromatase inhibitors. They also recommend treatment with bisphosphonates for patients with bone mineral density T score <2.5.

The use of aromatase inhibitor for treatment of endometriosis should be in addition to other medications to suppress ovarian hormones including birth control pills, GNRH agonist or any progestogen. In order to protect the bones, patients must use vitamin D with calcium and bisphosphonates to prevent the occurrence of osteoporosis.

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