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Goserelin acetate for recurrent endometriosis

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Abstract

Background Endometriosis is a chronic and recurrent disease characterized by the presence and proliferation of functional endometrial glands and stroma outside the uterine cavity. GnRH analogues are currently one of the most widely used medical therapies for endometriosis.

Objective This study assesses the role of zoladex (goserelin acetate depot) for patients with recurrent endometriosis after surgical treatment.

Methods A descriptive follow up study of 20 women with recurrent endometriosis after surgery were arranged to receive Goserelin acetate (Zoladex) one month depot administered subcutaneously monthly for a period of six months followed by one year follow up in AL- Karama Teaching Hospital -Wasit Governorate/ Iraq from May 2008 until May 2010.

Results Ninety percent of patients showed symptomatic improvement, ultrasound improvement achieved in 80%, recurrence rate of 20% within one year after stopping treatment and none of the patients required surgical interference during the period of the study.

Conclusions Our results support the beneficial role of Goserelin acetate (3.6 mg) month depot administered subcutaneously in the treatment of recurrent endometriosis after surgery.

Keywords Endometriosis, GnRH analogues, Goserelin acetate

Introduction

Endometriosis is a chronic and recurrent disease characterized by the presence and proliferation of functional endometrial glands and stroma outside the uterine cavity .It is estimated to occur in up to 10% of women of reproductive age [(1)]. Although endometriosis is seen primarily among women of reproductive age, this disease also can affect post-menopausal women and adolescents especially adolescents with uterine abnormalities, in particular, women with Müllerian anomalies resulting in outflow obstruction (increasing retrograde menstrual flow), as well as women with prolonged menstruation and shorter cycles (27 days or less) [(1)]. However, retrograde menstruation can be observed in up to 90% of women, suggesting the involvement of additional factors in the implantation and growth of endometriotic lesions in women [(2)].

Susceptibility to endometriosis is thought to depend on the complex interaction of genetic, immunologic, hormonal and environmental factors [(3)]. Endometriosis appears to be a multifactorial genetic disorder, in which allelic variants of many genes (including cancer susceptibility genes and genes coding for cytochrome P450 enzymes, nuclear receptors and immunologic mediators) can predispose women to develop endometriosis, depending on environmental conditions [(3)]. The growth of endometriotic lesions is also estrogen dependent, with lesions becoming inactive and gradually undergoing regression during states of ovarian down-regulation, such as amenorrhoea or menopause [(4)].

Pelvic pain associated with endometriosis generally is cyclical, the pain may become continuous as the disease worsens. The most common symptoms of endometriosis are dysmenorrhoea, dyspareunia and chronic non-menstrual pain. If endometriotic lesions affect the bladder or rectum, pain may also occur during micturition or defecation [5].

Infertility is a problem for many women with this disorder, the mechanisms of endometriosis-associated infertility still are not completely understood, generally, it is agreed that the most advanced stages of endometriosis are strongly correlated with infertility, particularly if pelvic adhesions distort normal pelvic anatomy and impair tubo-ovarian function [6].

Endometriosis also negatively impacts women's quality of life. A decreased quality of life may result not only from the symptoms of pelvic pain and infertility but also from the effects of various medical and surgical treatments [7].

Diagnosis of endometriosis can be difficult, given the non-specific nature of many of its symptoms, the common occurrence of pelvic pain in women without endometriosis and the considerable overlap with other conditions (e.g. pelvic inflammatory disease or irritable bowel syndrome) For this reason, a diagnosis can be confirmed only by a surgical procedure (generally laparoscopy) to excise and histologically evaluate disease implants [5,8].

In addition to relieving pain, the goals of treatment for patients with endometriosis are to prevent or delay disease progression by reducing endometriotic implants through surgical treatment or medically induced atrophy of the implants [8]. Neither medical nor surgical treatments have been proven to improve fertility rates and because of the chronic nature of this disease, long-term or repeated courses of medical therapy are required to control these symptoms [9].

Currently available medical therapies for endometriosis act by attempting to mimic periods during which a woman does not menstruate: menopause (GnRH analogues), amenorrhoea (chronic anovulation with danazol) or pregnancy [oral contraceptives (Ocs) or progestins] [5].

GnRH analogues are currently one of the most widely used medical therapies for endometriosis. These agents induce medical menopause by down-regulating hypothalamic-pituitary GnRH receptors, thus causing decreased gonadotropin secretion, suppression of ovulation and reduced serum estrogen levels. Several GnRH analogues used for the treatment of endometriosis include nafarelin, buserelin, histrelin, goserelin, triptorelin and leuprolide [10].

Methods

A descriptive follow up study performed in AL-Karama Teaching Hospital -Wasit Governorate/ Iraq from May 2008 until May 2010. The study included 20 women already diagnosed with endometriosis (endometrioma) in whom the diagnosis was confirmed by histopathological study after surgical exploration and presented with recurrence after surgery.

Recurrence defined as recurrence of symptoms (dysmenorrhea, dysparunea, pelvic pain or indurations on examination and complex ovarian cyst identified by ultrasonic examination (Semen's ultrasound machine) within a year of follow up. Exclusion criteria included patients who received any hormonal treatment for endometriosis postoperatively or lost their follow up during the period of treatment and follow up. All patients gave signed informed consent before inclusion in this study and arranged to receive Goserelin acetate (Zoladex) depot injection (3.6 mg) subcutaneously in the lower abdomen every 28 days for 6 cycles [11] and each patient had at least 1 year follow up after treatment. Follow up included monthly abdominal and pelvic examination and ultrasound examination.

Results

Twenty patients with recurrent endometriosis included in this study, their age ranged

between 30 and 42 years (mean 34), and parity (0-1). Symptomatic improvement where noticed in 18 patients (90%); 12 of them (60%) after the second injection. However the improvement on abdominal and pelvic examinations were noticed in 15 patients (75%) during the same period and raised to 85% (17 patients) after finishing the course of treatment (Table 1).

Table 1. The distribution of patients according to symptomatic improvement

Improvement	Number	Percentage
Improved	18	90%
Not improved	2	10%
Total	20	100%

Ultrasound examination showed complete resolution of endometrioma in 16 patients (80%) and improvement in ultrasonic features in the remaining 4 patients (20%); (Table 2).

Table 2. The distribution of patients according to radiological changes

Radiological changes	Number	Percentage
Total resolution	16	80%
Improvement	4	20%
Total	20	100%

Recurrence after stopping the treatment was recorded in 2 patients (10%) within the first 6 months and 2 patients (10 %) in the second half of the year (Table 3).

Table 3. The distribution of patients according to recurrence

The recurrence	Number	Percentage
Recurrent endometriosis	4	20 %
No recurrence	16	80%
Total	20	100 %

Side effects were recorded during the period of treatment including hot flushes in 12 patients (60%), sweating in 5 patients (40%), and bone pain in 4 patients (20%), a reduction in breast size in 4 patients (20%); (Table 4).

Table 4. Side effects recorded during the period of treatment

Side effect	Number	Percentage
Hot flashes	12	60%
Sweating	5	40%
Bone pain	4	20%
Decrease in breast size	4	20%

Pregnancy was recorded in 3 patients (15%) after finishing the treatment; however only one of them succeeded to finish the pregnancy and result in a live birth rate of (5%).

Discussion

Endometriosis is a common debilitating disease occurring in 1–5% of premenopausal women with a prevalence of 38.5% in infertile women and 5.2% in fertile women [12]. The medical management of endometriosis depends on the stage of the disease, the severity of symptoms, the age of the patient, and the future fertility intentions. The most widely utilized treatment modalities are expectant management, surgery, induction of a pseudopregnancy state with hormonal therapy, and induction of a pseudomenopausal state [13]. Six months of GnRH agonist therapy immediately following surgery reduces the rate of symptom recurrence, and increases the length of time before symptoms recur. It is also more effective in managing endometriosis-related pain after surgery than using oral contraceptives in the same way. The benefits may be particularly relevant for women with active peritoneal disease [11, 14].

In this study 20 women with recurrent endometriosis after surgery were arranged to receive Goserelin acetate depot injection each 28 days for six months, symptomatic improvement achieved in 90%, and radiological improvement in 80%, 20 % recurrence and 15% pregnancy rate. In the study of Reichel and Schweppe [15] the total subjective score and total pelvic symptom score showed a reduction by 86% and 93%, respectively, 54% of the patients showed a reduction of implants and adhesions by at least 50% or more, and 31.5% had a complete resolution of visible deposits. The mean reduction of implants and adhesions was 50%, 72% respectively. Twenty of 64 (31.3%) previously infertile patients successfully conceived within 12 months after discontinuation of the therapy [15]. Shaw [16]; concluded that the monthly administered 3.6-mg depot preparation of goserelin was highly effective at inducing resolution of endometriotic implants and relieving the symptoms of endometriosis with prevention of their return during 24 weeks follow-up in the majority of patients. However, results were not significantly different from those achieved with danazol 600 mg/d [16].

While in the study of Soysal et al [17] six months of treatment with anastrozole and goserelin as compared to goserelin alone increased the pain-free interval and decreased symptom and recurrence rates in patients following surgery for severe endometriosis. Furthermore, menopausal quality of life at 2 years after medical therapy remained unaffected [17].

However, adverse effects reported by women receiving GnRH agonist treatment are those of secondary hypogonadism (hot flushes, sweating, vaginal dryness, etc..). Furthermore, this treatment induces a dramatic decrease in bone mineral density (BMD) higher than in the early months of natural menopause, reaching 4-5% at the lumbar spine in 6 months, this bone loss has been found to be reversible in most studies. These adverse effects limit the duration of treatment in diseases that are chronic or recurrent by nature [18].

Side effects were recorded during the period of treatment including hot flushes in (60%), sweating (40%), bone pain in 4 patients (25%), decrease in breast size in (20%) otherwise no other serious side effects occurred. In the study of Fernandez et al [14], the incidence of adverse events was 97.4% with a mean number of 8.3 adverse events per patient; the main reported side effects were hot flushes and headaches, the adverse events resulted in discontinuation of the study for 10 patients, among the main side effects were one case of sciatalgia, one case of asthenia, and two psychotic depression events in the same patient [14].

Conclusions

Our results support the beneficial role of Goserelin acetate 3.6 mg depot injection each 28 days for 6 months in the treatment of recurrent endometriosis after surgery.

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