MEDICAL TREATMENTS FOR ENDOMETRIOSIS

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Introduction

Endometriosis is surgically treated upon diagnosis, but with a high rate of recurrence, suggesting that a combination of surgical and medical management might provide better outcomes (1). The current medical treatment of endometriosis is based on ovarian hormone, suppression that induce atrophy of endometrial implants and interrupt the cycle of stimulation for obtaining iatrogenic menopause.

Hormonal drugs causing iatrogenic menopause

The use of GnRH agonists is well recognized (3), but new GnRH antagonists are equally effective for regression of size and histological components of endometriosis. On this basis, GnRH antagonists may be considered an alternative choice instead of GnRH agonists for the treatment of endometriosis, since they have fewer side effects (i.e. postmenopausal symptoms) and no estradiol add-back is needed (3). Available GnRH antagonist formulations require subcutaneous administration at least once a week, but data are still limited. Furthermore the development of new orally available GnRH antagonist (NBI-42902) that immediately suppress the reproductive endocrine axis reducing the LH and FSH levels followed by a delayed suppression of E2 may have future clinical utility in endometriosis treatment (4-6).

Similarly, aromatase inhibitors may cause a iatrogenic menopause effect; the use of aromatase inhibitors for endometriosis is still experimental and is based on the observation that endometriotic lesions express the enzyme aromatase and are able to make their own estrogen, even in the absence of gonadotropin stimulation (7). Pain relief after 6 months of daily treatment with an aromatase inhibitor together with high-dose norethindrone acetate or an oral contraceptive and showed significant resolution of pelvic pain in women with endometriosis (8, 9). Further researches are required to determine if aromatase inhibitors will be safe and effective for long-term use in women with endometriosis pain (10).

Recently, the evaluation of selective estrogen receptor modulators (SERMs) efficacy suggested that bazedoxifene (BZA), currently under evaluation for the treatment of osteoporosis, may be superior to other SERM in endometriosis treatment in vitro. The regression of endometriotic lesions appears to have occurred primarily by suppression of estrogen-induced proliferation and further experiments using animal models as well as clinical trials will be helpful in determining the utility of this compound in women with endometriosis (11).

Hormonal drugs causing pseudopregnancy

Current hormonal management of endometriosis is based also to the creation of a pseudopregnancy state; in this context the efficacy of progestins and oral contraceptives is well-known, but the introduction of new formulations and molecules create new advances. Danazol was once the gold standard of endometriosis treatment, but has been used less because associated with androgenic side effects and not tolerable long-term treatment.

The effectiveness of danazol by vaginal route for 12 months on dysmenorrhea, dyspareunia and pelvic pain has been demonstrated, with few side effects (12).

Recent advances concentrated also on the efficacy of dienogest, a novel progestin that may represent a safe and effective long-term treatment option for women with endometriosis (13). Dienogest (2 mg/day for 12 weeks) showed a significant efficacy in pain reduction, in comparison with placebo and with gonadotropin-releasing hormone agonists (leuprolide acetate) with less adverse effects (14). Likewise, oral contraceptives assumed a new role in treatment endometriosis since their use is not limited to the preoperative treatment, but the post-operative use is now considered an essential part of long-term therapeutic strategies. Continuous administration, without a 7-day break, to avoid withdrawal bleeding, may be more beneficial in terms of pain relief. Their effect is limited to the period of use, with a significant reduction of endometriosis lesions and pelvic pain recurrences (15,16). A regression of endometriosis lesions has been observed in vitro with administration of selective progesterone receptor modulators (SPRMs) (17,18). SPRMs may offer new insights in hormonal therapies (19).

Non-hormonal agents

Increasing knowledge about the pathogenesis of endometriosis is providing the opportunity to use new non-hormonal agents for medical treatment, including antiflammatory, antiangiogenetic and pro-apoptotic compounds. Since endometriosis is characterized by an altered endometrial production of inflammatory mediators, included omega-3 polyunsaturated fatty acids, their therapeutic effect has been suggested. Omega-3 fatty acids (DHA and EPA) have been shown to significantly reduce interleukines and prostaglandins release, decrease Cox-2 expression, suggesting a potential benefit in treatment of pelvic pain in patients with endometriosis (20). The advances in diagnosis and treatment of endometriosis will improve delivery of care for patients with endometriosis and these are a research priority.

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