Dienogest in the Treatment of Endometriosis

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Abstract
Endometriosis is a prevalent chronic disease in up to 10% of women of reproductive age and often causes pain symptoms. In some patients, these symptoms negatively affect quality of life for a long time. Dienogest is an oral progestin that was recently approved for the treatment of endometriosis. It is allowed for long-term administration with a favorable safety and tolerability profile. Dienogest 2mg/day was superior to placebo in relieving pain symptoms in patients with endometriosis, equivalently effective to gonadotropin releasing hormone agonist (GnRHa). The size of endometriomas was reduced by use of dienogest. Postoperative administration of dienogest showed the efficacy in relieving pain and suppressing recurrence of endometrioma in patients with endometriosis. Dienogest was also effective in relieving symptoms in women with deep infiltrating endometriosis (DIE) or extragenital endometriosis. Dienogest is an alternative for the treatment of endometriosis because of its efficacy, safety and tolerability.

Keywords: Dienogest; Endometriosis

Abbreviations: GnRHa: Gonadotropin Releasing Hormone Agonist; DIE: Deep Infiltrating Endometriosis;

Introduction
Endometriosis is a common disease in up to 10% of women of reproductive age. It often causes symptoms such as dysmenorrhea, chronic pelvic pain, dyspareunia and dyschezia [1]. It is also associated with ovarian endometrioma which requires surgery for both diagnosis and treatment. However, recurrence rates are approximately 30-50% within 5 years after surgery [2]. Dienogest is a new synthetic oral progestin that was approved for the treatment of endometriosis [3].

It works by preventing the growth of the endometrium and suppressing estrogen production [4]. Additionally, it is allowed for long-term administration unlike gonadotropin releasing hormone agonist (GnRHa) [5]. Long-term dienogest showed a favorable safety and tolerability profile, including a low incidence of hyposexual effects and minimal change in bone mineral density [6]. The aim of this study is to review literature and assess the efficacy of dienogest in the treatment of endometriosis.

Pain Relief
In a 12-week randomized placebo-controlled study involving 198 women, dienogest 2 mg/day was more effective than placebo for reducing endometriosis-associated pelvic pain [7]. A study of one year-treatment demonstrated that dienogest showed pelvic pain reduction through the treatment period [5] and the decrease of pelvic pain persisted for at least 24 weeks after treatment cessation [8]. Dienogest 2mg/day for 24 weeks was equivalently effective to subcutaneous leuprolide acetate 3.75 mg every 4 weeks [9] or intranasal buserelin acetate 900mg/day [10] in relieving the painful symptoms of endometriosis.

Postoperative administration of dienogest showed a significant higher pelvic pain reduction than the expectant management group until 24 months of follow-up in a multi-center study [11]. Dienogest prevented pelvic pain recurrence as effectively as GnRHa after laparoscopic surgery for endometriosis [12]. Dienogest plus estradiol valerate is significantly more effective than levonorgestrel-releasing intrauterine device in reducing pelvic pain after surgery for endometriosis [13].

Ovarian Endometrioma
Treatment of dienogest over 12 months decreased the size of endometrioma to approximately 30% of the initial sizes [14] and the similar effect was also observed in the patients of recurrent endometrioma [15].

There has been reported the efficacy of postoperative dienogest on endometrioma recurrence. A postoperative dienogest treatment versus a control group showed a significant difference in recurrence at 12 (0% vs.16.5%) or 24 months (0% vs. 24.0%) [11]. Although recurrence was not seen in patients...
with dienogest, no medication group showed recurrence up to 50% at 5 years after surgery [16]. No significant difference was observed in the postoperative recurrence rate between the dienogest and goserelin (subcutaneous 1.8 mg every 4 weeks) group [17].

### Deep Infiltrating Endometriosis (DIE)

DIE can affect the bowel and the urinary tract and causes severe pain. Dienogest is as effective as surgical treatment in relieving pain in more than 90% of women with DIE at one year follow-up [18]. Postoperative administration of dienogest significantly reduced the endometriosis-related pain in the DIE patients [19]. A prospective cohort study demonstrated that dienogest for 12 months was effective to control pain related to DIE, even without reducing the volume of DIE nodules [20].

### Extragenital Endometriosis

There are a few pilot studies describing the efficacy of dienogest on extragenital endometriosis. Four cases with colon endometriosis, treated with dienogest for over 6 months, exhibited their size reduction and pain relief related with the lesions [21]. By treatment of dienogest for 12 months, symptoms were improved and the nodules reduced in size in 6 cases of bladder endometriosis [22].

### Conclusion

The above studies suggested that dienogest is an alternative as first-line therapy for relieving pain and suppressing recurrence in patients with endometriosis. However, there is still a need to establish the effect of long-term treatment with dienogest and the recurrence after its discontinuation. Moreover, there were no studies comparing the efficacy and safety between dienogest and combined oral contraceptives which are also effective in the treatment of endometriosis. Further randomized investigations are necessary to elucidate strategies of dienogest for the treatment of endometriosis.

### References
