Endometriosis and its treatment options comparison with dienogest

*L.Karpagavalli1, M.Vigneshwar2, S.Charumathi2

1 Jaya College of Paramedical Sciences, Thiruninravur, Chennai-602 024, Tamil Nadu, India.
2 Aadhi Bhagawan College of Pharmacy, Rantham Village, Thiruvannamalai Dist, Tamil Nadu, India.

Abstract
Endometriosis is one of the most common worldwide encountered benign disease in women. Endometriosis is seen in various sites of the body along with intense pain (dysmenorrhea, dyspareunia). It also leads to infertility in more than 35% patients in reproductive age. Today’s treatment options are double edged sword due to various adverse effects of the drugs. Dienogest appears to be more effective in treating endometriosis along with superior safety and tolerability.

Key words: Endometriosis, Dysmenorrhea, Dyspareunia, Dienogest.

INTRODUCTION
Endometriosis is an enigmatic disease which is seen in women [1]. Endometriosis is abnormal growth of endometrium like tissue outside of the uterus primarily on the ovaries which causes inflammatory reactions and leads to formation of scar tissue [2]. The Early diagnosis endometriosis remains as a tough contest. The treatment or management also becomes a double edged sword due to various drugs having various adverse effects. Even the surgery also has certain drawbacks where there is chance of recurrence of the disease. Hence there is a requirement to find the most rationale approach to the management of disease [3].

Epidemiology
Endometriosis may affect any female, from pre-menarche to post-menopause. Worldwide the number of women affected is between 6–10% [4]. It is common in women with infertility and chronic pelvic pain (35–50%). Endometriosis seen in about one intenwomen of reproductive age.

PATHOPHYSIOLOGY OF ENDOMETRIOSIS
The exact cause remains unknown, while the most widely accepted theories of endometriosis are as follows

1. Theory of retrograde menstruation
During menstrual flow, some endometrial cell debris exits by entering fallopian tubes and gets itself attached to the peritoneal surface, where it can grow and form an endometrial growth.

2. Theory of Müllerianosis
According to this theory some cells which are capable of developing to endometrial cells migrate downward at 8th -10th week of embryonic life and will become as seeds for endometrial growth.

3. Environmental toxins
The toxins like Dioxin, nickel etc..may cause endometriosis.

4. Coelomic metaplasia:
Coelomic cells are those which have the common ancestor of endometrial & peritoneal cells which may transform as one type of cell to the other, perhaps triggered by inflammation.

Location
Most often occur in following places: Peritoneum, ovaries, fallopian tubes, vagina, cervix, rectum, Cul-de-sac etc.

Signs and symptoms
- Heavy menstrual period,
- Frequent Premenstrual pain,
- Abnormal Bleeding between periods,
- Heavy pelvic pain,
- Intense Painful menstrual cramps,

To whom correspondence should be addressed:
L.Karpagavalli
Email: karpagavalliev@gmail.com
• Pain severely seen in intestine, lower abdomen,
• Chronic fatigue [3]
• Extreme Painful bowel movements or pain during urination.

DIAGNOSIS

Ultrasound
By Use the pelvic ultrasound onemay identify larger grown Endometrioma. But, smaller endometriomas cannot be identified by this technique.

Laparoscopy
It is a surgical procedure in which a visualizer is used to see inside of the abdominal cavity, this is the only official way to diagnose because visualization of lesions is directly seen.

Biopsy
Biopsy is in which the small portion of tissue is excised if the visualization of lesion is not possible.

Management of Endometriosis
Currently there is no cure for endometriosis as even after the surgery the recurrence is seen. It can be only managed by
1. Management of pain
2. Endometriosis associated infertility.

Contraceptive Therapies
OCP or COC are off- labelled use (not approved for this indication) because of lack of trial. They also only prevents the growth of endometriosis by eliminating menstrual flow.
Disadvantages;
1. Break through bleeding (BTB)
2. COCs includes both inhibition of endometrial growth but also has a protective effect against lesion necrosis [7].

Androgenic Steroids
It includes Danazol which increases the androgen level in the system thereby inhibits the growth of endometrial lesions.

Disadvantages
1. Hirsutism and Acne [8]
2. Vaginal dryness.
3. Weight gain.
4. Breast atrophy [9]

GnRH Agonists
It includes leuprolide, Goserelin etc. which down regulates the GnRH and helps in reducing the endometrial growth but it has severe adverse effects which now received a BLACK BOX WARNING by US FDA.
Disadvantages
1. Its adverse effects are hypoestrogenism,
2. Demineralization causing Low BMD [10].
3. Increasing the chance of CVD etc.

PROGESTINS
There are different types of Progestin’s used in the Management of endometriosis and symptoms associated with it they are

MDPA
Medroxyprogesterone acetate (MDPA) is used very often it Works By acting as an Gonadotrophin antagonist and by decreases the growth of endometriotic stromal cells but it is Less Progestogenic when compared to DNG.
DISADVANTAGES
1. Decrease in BMD.
2. Hypo-Estrogenism,
3. Delayed return to fertility (according NFI report)
4. Immunosuppression.

NETA
Norethisterone acetate (NETA) or Norethindrone is a gonadotrophin antagonist, it also reduces the growth of endometrial Cell and associated pelvic pain but it has less Progestogenic action when compared with DNG.
Disadvantages
1. BTB
2. Hot flushing
3. Vaginal dryness.
4. Low patient compliance
Considering the all above molecules the adverse effects are very high which resembles a double edged sword. Hence a new molecule with superior safety, efficacy and tolerability is now available.

DIENOGEST (DNG)
Dienogest is a 19-nortestosterone progestin group. It has the combined characters of both nortestosterone and progesterone derivatives. Its half-life is just 10 hours this means there is no risk of accumulation most of the drug is excited in urine within 24 hours. Dienogest has strong progestogenic effects on the endometrium. It is the only progestin which does not possess an
androgenic effect but anti-androgen activity. It also induces optimum Decorin (an ubiquitous proteoglycan [15]) along with anti-proliferative, anti-Angiogenic and anti-cytokin effect. It reduces endometrial stromal growth by paracrine fashion and also prevents the cell proliferation. It has less adverse when compared with other class of progestins and also possess superior safety [12] and tolerability [13].

Advantages
1. It also has 90% oral bioavailability,
2. It has 77% patient compliance,
3. Bleeding frequency and intensity reduced along with cyclic pattern resumed in 3-4 weeks,
4. Better pain control,
5. Rapid resumption to ovulation (within 15-41 days) [14].

CONCLUSION
Considering the various adverse effects of the current treatment options and their ineffectiveness in treating the endometriosis a newer molecule approach becomes most essential for most appropriate treatment to the endometriosis. Now the molecule with unmatched efficacy and lesser adverse effect for the treatment of Endometriosis is Dienogest because of its distinct properties. Thus Dienogest appears to be a more effective drug in the management of endometriosis.

CONFLICT OF INTEREST
No conflict of interest.

REFERENCE