

Endometriosis : An Enigmatic Disease

Endometriosis, a recognized clinical condition, is associated with pain and subfertility in 10-15% of women of the reproductive age group globally¹. The pathophysiology of this disease still remains elusive. The varied clinical presentations of the disease and the immense impact it has on the physical, psychological, domestic, social and professional lives of those suffering from it put challenges on the treating gynaecologists to find a solution to this perplexing problem. Currently clinical diagnosis and medical treatment are the pillars of management of symptomatic endometriosis only giving way to surgical intervention if the conservative methods are inadequate. Artificial Reproductive Techniques (ART) should be the preferred approach in associated subfertility.

Pain is the hallmark of the disease. Most of the patient with endometriosis present with dysmenorrhoea, dyspareunia, dyschezia, lower abdominal and pelvic pain, either alone or in combination with subfertility. The classical triad of pelvic endometriosis is progressive dysmenorrhoea, dyspareunia and heavy menstrual bleeding. Therefore, in majority of cases the diagnosis is made clinically. However, 30-40% of pelvic endometriosis also present with ovarian endometrioma where pelvic ultrasonography and MRI may become helpful. Laparoscopy is no more a gold standard for the diagnosis of endometriosis in modern medicine. Serum biomarker like CA125 does not have any diagnostic or prognostic value in the disease management.

Medical management is the mainstay of treatment in endometriosis associated pain. It is also useful in pre-operative and post-surgical adjuvant therapy as well as in adolescent disease. Out of these, Pre-operative medical therapy is used in severe endometriosis for better surgical dissection in restoration of the pelvic anatomy. However, it has not been shown to have any immediate improvement on the outcome of pain. On the other hand, post-operative adjuvant therapy is known to have positive impact on immediate pain relief. It has also been shown to be very useful in the prevention of recurrent disease. Hence, it should be offered to every postsurgical patient where pregnancy is not desired. Symptomatic relief of pain associated with endometriosis can be achieved by NSAIDs, SSRIs and antidepressants without any effect on the progression of the disease. A basket of hormonal preparations containing Progestogens (oral/injectables/implants), Combined Oral Contraceptives (COC) pills, GNRH agonists and antagonists, aromatase inhibitors and danazol are available. COC pills either cyclical or continuous are known to work as long term medical therapy in endometriosis and has been shown to significantly reduce dysmenorrhoea, dyspareunia, dyschezia and cyclical pelvic pain². Continuous COC pills however, work better in dysmenorrhoea than cyclical pills. Combined

contraceptives used via other routes eg, transdermal or vaginal are also equally effective³. This group of hormonal preparations are also effective in long term use for secondary prevention of recurrent disease. Progestogens are available in oral (Medroxyprogesterone Acetate / Dienogest) Injectable like Depo-Medroxyprogesterone Acetate (DMPA), and as implant such as Implanon /Levonorgestrel releasing-Intra Uterine System (LNG-IUS). Continuous Progestogens and anti-progestogen (Gestrinone) are equally effective. Out of all Progestogen preparations Oral Dienogest⁴ and LNG-IUS have been found to cause significant reduction of postoperative pain, comparable to GnRH agonist⁵. They are also more effective in reducing pain and/or disease recurrence with significantly higher patient satisfaction comparable to COC Pill and Danazol. Etonorgestrel releasing subdermal implant, like LNG-IUS has also been reported to cause significant reduction of endometriosis associated pain, dysmenorrhoea and chronic pelvic pain⁶. Amenorrhoea, irregular bleeding, acne, weight gain are usual side effects. Effect on BMD is a concern in long term use of DMPA. Danazol is no longer a preferred medical treatment of endometriosis because of its serious androgenic side effects. GnRH agonists (Leuprolide Acetate, Goserelin/Triptorelin/Nafarelin) are potent agents, equally effective as oral Dienogest and are known to reduce endometriotic implants with associated inflammation and adhesion. They can significantly reduce endometriosis associated pelvic pain and can cause delay in recurrence of the disease but shown to be less effective than LNG-IUS⁷. They are equally effective irrespective of route of administration. Add-back therapy is recommended to prevent side effects like vaginal dryness, hot flushes and loss of bone mineral density⁸. Aromatase inhibitors, Letrozole and Anastrozole do not have strong evidence to support their efficacy in endometriosis and should be reserved as the last option in the treatment of the disease.

The basic principle of **surgical treatment** of endometriosis is the removal or destruction of all endometriotic tissue including ovarian endometrioma, peritoneal implants and Deep Infiltrating Endometriosis (DIE). The main indication of surgical intervention in endometriosis is pain. Endometriotic implants are best treated by surgical excision than ablation⁹. There are convincing evidences to support surgical excision of ovarian endometrioma over drainage and coagulation¹⁰. However, any surgical excision of ovarian endometrioma has its negative impact on ovarian reserve and this has to be thoroughly explained to the patient before

surgery. Sub-fertile patient trying for pregnancy should not have surgical excision as first line of therapy unless she is in pain or the endometrioma is large enough to make ovum pick up difficult. Pelvic denervation by Presacral Neurectomy (PSN) has been reported as an effective procedure in reducing pain in recurrent endometriosis following first-line surgical treatment. However PSN can be associated with denervation of bowel and bladder causing constipation and urinary dysfunction¹¹.

Deep Infiltrating Endometriosis (DIE) extends beneath the peritoneum and may affect the uterosacral ligaments, pelvic side walls, rectovaginal septum, vagina, bowel, bladder, or ureter. Excision of these nodules is usually performed when surgical treatment is chosen. The extent of surgical excision of DIE depends on the organ involved and the depth of infiltration and can lead even upto bowel resection. Hence DIE is best managed by multidisciplinary approach in tertiary referral centres.

Increased incidence of **subfertility** associated with Endometriosis is best treated with artificial reproductive techniques. Pre- and Post Operative medical treatment does not enhance the outcome of subfertility treatment and is not recommended. Repeated surgery for recurrent ovarian endometrioma can hamper the fertility outcome¹². However, if surgery is needed for subfertile patients, as in the above mentioned conditions, post operative ART should be considered sooner.

Endometriosis is being recognised more frequently as a cause of abdominal pain and dysmenorrhoea in adolescents. The Gynaecologist has to be "Endometriosis Minded" to make an early clinical diagnosis and try to arrest disease progression. Laparoscopy is not appropriate for diagnosis. Combined oral contraceptive pills¹³ and progestogens like Dienogest¹⁴ are effective as first line of treatment in **adolescent endometriosis**. NSAIDs can be used for pain relief liberally for symptomatic relief. GnRH analogue usage should be reserved only for second line therapy due to its adverse effects.

Endometriosis is known to be a benign disease. However, endometriosis is associated with increased risk of ovarian cancer specially Clear cell carcinoma and Endometrioid carcinoma.

Endometriosis is common in the reproductive age group. However, nowadays endometriosis is being diagnosed in adolescent girls. Hence, clinical diagnosis should be encouraged followed by first line medical treatment. Complete Surgical treatment should be reserved for resistant cases only. Subfertility is best treated by ART.

As endometriosis remains an enigmatic disease collaborative scientific efforts and research fundings should be directed towards the disease to seek a cure for the same.

FURTHER READINGS

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