

Endometriosis Diagnosis and Management in Adolescent Patients and Current Treatment Regimes

Ashish Ashish¹, Kusum Kusum², Sangeeta Rai³, Radha Chaube², Shivani Mishra¹, Royana Singh^{1, *}

¹Department of Anatomy, Institute of Medical Science, Banaras Hindu University, Varanasi, India

²Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi, India

³Department of Obstetrics & Gynaecology, Institute of Medical Science, Banaras Hindu University, Varanasi, India

Email address:

royanasingh@bhu.ac.in (R. Singh)

*Corresponding author

To cite this article:

Ashish Ashish, Kusum Kusum, Sangeeta Rai, Radha Chaube, Shivani Mishra, Royana Singh. Endometriosis Diagnosis and Management in Adolescent Patients and Current Treatment Regimes. *Reports*. Vol. 1, No. 2, 2021, pp. 10-13. doi: 10.11648/j.reports.20210102.11

Received: February 20, 2021; **Accepted:** March 15, 2021; **Published:** July 9, 2021

Abstract: Endometriosis disease affects about an estimated number of 176 million women worldwide, which constitutes ~10% of the total female population causing debilitating symptoms of pelvic pain and infertility, thus limiting the quality of reproductive life of an affected woman. Progestins now have become a mainstay of endometriosis suppression, out of which dienogest has been opted as a best option worldwide. Its an expertise literature review with recommendations on the use of dienogest in the context of various clinical considerations when treating endometriosis disease. Experts have reviewed and included those, which they found to be considered most relevant in clinical practices, based on their own clinical experiences. Long-term uses (>15 months) of dienogest for the management of endometriosis is presented, with experts concluding that the efficacy of dienogest must be assessed primarily for its impact on pain and quality of life of a woman. Fertility preservation, avoiding or delaying surgery, and managing the bleeding irregularities occurring because of this medical treatment are also considered here. Counseling women on potential bleeding risks before starting the treatment may be helpful, as the evidences suggest that few of them discontinues the treatment because of this reason outweighing the benefits. Overall, the evidences demonstrate that dienogest offers an effective and tolerable alternative in adjunct to surgery and provides many advantages over combined hormonal contraceptives for the treatment of endometriosis. But its important for all that treatment guidelines must be followed strictly with great care and must be tailored to the woman's individual needs and their desires.

Keywords: Adolescents, Dysmenorrhea, Endometrioma, Endometriosis, Pelvic Pain

1. Introduction

Endometriosis is a chronic inflammatory disease condition in women, where tissues resembling endometrium, usually stromal or glandular, are located outside the uterine cavity [1]. Menorrhagia, dysmenorrhea, dyspareunia, dyschezia, dysuria, pelvic pain and infertility are the prominent symptoms seen in endometriosis suffering women [2]. In addition, factors like environmental and dietary elements, immune system, viz. cytokines, interleukins, and intrinsic anomalies in endometrium are also associated with the disease [3, 4] Many previous studies have assessed the risk factors associated with endometriosis [4]. Age, race, alcohol usage, body mass index, cigarette smoking, and menstrual characteristics such as early age menarche, menstrual length, cycle regularity,

dysmenorrhea, and menstrual flow intensity are all associated with the incidences of endometriosis [5]. Globally, one in ten women during their reproductive years (between puberty and menopause) are having endometriosis [6], which is about 176 million women population worldwide suffering from the disease [6]. Its partially explained by the facts that gold standard for endometriosis disease diagnosis requires a direct visualization of lesions during surgery, duly followed after histological confirmation of endometrial glands and stromal tissues in biopsies of suspected implanted lesions [7]. Additional factors that contribute to diagnostic delay are treatment of pain with oral contraceptives or nonsteroidal anti-inflammatory drugs and assumptions of dysmenorrhea as a normal event [6]. Disease treatments are limited to hormonal therapies with many side-effects and complicated

surgical removal of disease often need to be repeated. Retrograde menstruation is a widely accepted theory and Dr. John Sampson explained the disease pathogenesis [8]. This sampson's theory suggests that during menstruation, uterine tissue contracts and menstrual tissues flow back through the fallopian tubes instead of out of the body and implants at various sites, most commonly in the pelvis, oviducts and peritoneal cavity [8]. It well known that 76-90% of all women experience this endometrial debris, including both epithelial and stromal cells [9]. However, only in endometriosis patients, this menstrual tissue is able to adhere on peritoneal structures, develops a blood supply and grows into an endometriotic lesion [10]. It's likely to say that women who develops endometriosis must have a genetic, biochemical or immune system dysfunction, which does not allows the removal of menstrual debris, rather facilitates menstrual tissue adhesion to peritoneum and endometriotic lesion formation [11]. Now its well known that women with endometriosis exhibit immune dysfunction in a form of local and systemic inflammation [12, 13]. More specifically, in plasma and peritoneal fluid (PF), endometriosis patients display an aberrant number of immune cells, cytokines and chemokines, thus promoting an inflammatory environment compared to healthy women [2, 14, 15]. And this inflammatory environment has also been a contributing factor for chronic pelvic pain and infertility experienced by patients [16, 17]. A significant proportion of adolescent girls suffer with endometriosis but diagnostic delay is very common, partially due to the differences in clinical presentation compared to adults [18]. Delay in the disease diagnosis, explains severity of the disease affecting to younger patients and supports for the need of a simple, non-invasive tool for its screening [19, 20]. It's very important for physicians to recognize endometriosis in younger patients, so far timely treatment can be given to them. For it, patients presenting dysmenorrhea and chronic pelvic pain should not be underestimated, and a detailed history must be obtained before performing any clinical evaluation and pelvic sonography [21]. Furthermore, in adolescent patients, clinicians must focus on non-invasive diagnosis rather than surgical or laparoscopy. Diagnosis of endometriosis can provide some reassurance to adolescent patients regarding the causes of their pain. It may causes anxiety as it requires a long-term treatment or surgery or can cause infertility and so, a scheduled frequent follow-up visits to clinicians is very important [22].

2. Classification Systems of Endometriosis

Numerous proposed systems now exist which classify various forms of endometriosis mainly exists in the American Society of Reproductive Medicine (ASRM) [23, 15]. But now it has been modified and renamed into Revised American Society for Reproductive Medicine classification of endometriosis (rASRM) [24]. All of these classification

systems divide endometriosis diseases into four stages, which are all based on the increasing severity of ovarian lesions, particularly the number of endometrial implants, their depth, and adhesions [25]. The stages are assigned on scoring system and these are as follows: Stage I : 1-5 points, indicates minimal disease i.e., few superficial implants [26], Stage II: 6-15 points, indicates mild disease which includes more and deeper implants, Stage III: 16-40 points, for moderate disease having many deep implants, small cysts on one or both ovaries and Stage IV: >40 points, indicate severe condition with many deep implants, large cysts on one or both ovaries with dense adhesions [27].

Diagnostic Management of Endometriosis Disease in Adolescent Patients

Current surgical treatments have a deleterious effect on ovarian follicle reserves and studies suggest a recurrence rate of about ~56% cases of endometriosis in adolescent patients [28]. Its now stands that conservative treatment approaches like surgery is desired to be avoided rather hormonal therapies and use of analgesics are recommended and preferred for relief of endometriosis-related pain. In a multicentre study for 52-week, dienogest (2 mg) has been found to be very effective in relieving the symptoms (pelvic pain, dysmenorrhea, and dyspareunia) and signs (pelvic tenderness and induration) of endometriosis in adolescent patients [29]. In addition to it, dienogest (2 mg) was generally found to be well tolerated and consistent with previous findings in endometriosis suffering adults. Given that adolescence is a crucial time for accumulation of BMD and data on the impact of endometriosis treatment at this age are of particular interest [30]. In adolescents treated with dienogest 2 mg for a year, a reduction of ~1.2% in BMD was observed from baseline to the end of the treatment. This slight reduction can be balanced against recovery of BMD once the treatment stops, and a significant reduction in endometriosis-associated pain was observed [30]. The impact of these observations in adolescent patients must be considered in context with the fact that BMD is only a surrogate marker for bone health. Important confounding factors must be considered in children and adolescent patient especially when performing DEXA, including variation in age, race, gender, puberty and height. Thus, bone density interpretation in children and adolescents can lead to significant aberrant diagnosis of osteopenia or osteoporosis, because of low BMD scores inferred from DEXA. In conclusion, although challenges with the interpretation of BMD in the adolescent population are recognized, still dienogest (2 mg) is a favorable owing, that may be because of the lack of alternative treatments, when one consider benefit over risk as priority [31].

3. Expert Recommendations

The occurrence of endometriosis and its symptomatic impact on one's health should not be underestimated in adolescent patients. Timely diagnosis and initiation of the disease treatment must be taken as early as possible.

Diagnosis of endometriosis via surgical interventions must be avoided in adolescent patients, in place of it one must favor clinical diagnostic methods (biochemical, hormonal or tumor biomarker) on the basis of patient's symptoms. Multiple treatment options are available for adolescent patients who are all suffering with endometriosis, but the use of dienogest (2 mg) has been found to be used prominently in the patient's population. However, decisions for the disease treatment are made on an individual basis and has a risk or benefit approach, but it must always consider efficacy and safety on its priority.

4. Conclusions

Endometriosis is a chronic gynecological disease and so far medical treatment be maximally advised while surgical interventions must be avoided and minimized unnecessarily. On behalf of surgical interventions, Dienogest (2 mg) offers an effective alternative for the long-term management of endometriosis disease. Furthermore, the evidences prove that patients willing accept the side effects like bleeding irregularities, often occurring with the medication of dienogest (2 mg), in place of giving a great relief from chronic pelvic pain [31, 32].

In clinical practices, there is always a need to counsel patients, regarding the expected side effects, efficiency and safety measures of each treatment approach taken by them. Its compulsory to follow the treatment guidelines to provide a tailored care according to each and every woman's needs and desires, and it's a very important component of any disease management strategies taken by clinicians.

Funding

The experiment had not received any kind of extramural research grant from any funding agency.

Declaration of Competing Interest

All the authors declare that there is no any conflict of interest.

Acknowledgements

This research was sponsored by Multi-Disciplinary Research Units (MRUs) and DST, a grant by ICMR-Department of Health Research [Grant No: 6004].

References

- [1] Acién, Pedro, and Irene Velasco. 2013. "Endometriosis: A Disease That Remains Enigmatic." *ISRN Obstetrics and Gynecology* 2013: 1–12.
- [2] Adaji, Enemona, Anand Ahankari, and Puja Myles. 2017. "An Investigation to Identify Potential Risk Factors Associated with Common Chronic Diseases among the Older Population in India." *Indian Journal of Community Medicine* 42 (1): 46–52.
- [3] Alio, L et al. 2019. "When More Is Not Better: 10 'Don'Ts' in Endometriosis Management. An ETIC* Position Statement." *Human Reproduction Open* 2019 (3).
- [4] de Almeida Asencio, Fernanda et al. 2019. "Symptomatic Endometriosis Developing Several Years after Menopause in the Absence of Increased Circulating Estrogen Concentrations: A Systematic Review and Seven Case Reports." *Gynecological Surgery* 16 (1): 1–11.
- [5] As-Sanie, Sawsan et al. 2019. "Assessing Research Gaps and Unmet Needs in Endometriosis." *American Journal of Obstetrics and Gynecology* 221 (2): 86–94.
- [6] Ashish, Ashish et al. 2021. 4 Acta Scientific Gastrointestinal Disorders *The Role of Oxidative Stress and Antioxidant Effects in Female Endometriosis: A Systematic Review*.
- [7] Ashish, Ashish, Kusum Kusum, Sangeeta Rai, and Royana Singh. 2020. "Endometriosis a Brief Review: Evaluation of Crucial Risk Factors and Current Treatment Regimes." *International Journal of Advances in Medicine* 7 (12): 1896.
- [8] Audebert, Alain. 2018. "Endometriosis." In *Encyclopedia of Endocrine Diseases*, MDText.com, Inc., 498–505.
- [9] Brosens, I., S. Gordts, and G. Benagiano. 2013. "Endometriosis in Adolescents Is a Hidden, Progressive and Severe Disease That Deserves Attention, Not Just Compassion." *Human Reproduction* 28 (8): 2026–31.
- [10] Bulun, Serdar E. 2019. "Endometriosis." In *Yen & Jaffe's Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management: Eighth Edition*, Elsevier Inc., 609–642. e7.
- [11] Carpinello, Olivia J et al. 2000. Endotext *Endometriosis*.
- [12] Donnez, Jacques. 2017. "Introduction: From Pathogenesis to Therapy, Deep Endometriosis Remains a Source of Controversy." *Fertility and Sterility* 108 (6): 869–71.
- [13] Ebert, Andreas D. et al. 2017. "Dienogest 2 Mg Daily in the Treatment of Adolescents with Clinically Suspected Endometriosis: The VISanne Study to Assess Safety in ADOlescents." *Journal of Pediatric and Adolescent Gynecology* 30 (5): 560–67.
- [14] Eisenberg, V. H., C. Weil, G. Chodick, and V. Shalev. 2018. "Epidemiology of Endometriosis: A Large Population-Based Database Study from a Healthcare Provider with 2 Million Members." *BJOG: An International Journal of Obstetrics and Gynaecology* 125 (1): 55–62.
- [15] Foti, Pietro Valerio et al. 2018. "Endometriosis: Clinical Features, MR Imaging Findings and Pathologic Correlation." *Insights into Imaging* 9 (2): 149–72.
- [16] Giudice, Linda C, and Lee C Kao. 2004. "Endometriosis." *The Lancet* 364 (9447): 1789–99.
- [17] Hsu, Albert L., Izabella Khachikyan, and Pamela Stratton. 2010. "Invasive and Noninvasive Methods for the Diagnosis of Endometriosis." *Clinical Obstetrics and Gynecology* 53 (2): 413–19.
- [18] Klemmt, Petra AB, and Anna Starzinski-Powitz. 2017. "Molecular and Cellular Pathogenesis of Endometriosis." *Current Women's Health Reviews* 13 (999): 1–11.

- [19] Kusum, Kusum et al. 2020. "Aromatase Gene Polymorphism (Rs2470152) in Polycystic Ovary Syndrome Patients of Eastern Uttar Pradesh Population." *Journal of Clinical and Diagnostic Research* 14 (10): 3–7.
- [20] Kusum, Rai S, and Chaube R. 2019. "Endometriosis: Role of Aromatase and Recent Advances in the Disease Treatment." *Austin J Obstet Gynecol* 6 (2).
- [21] Kyama, Cleophas M., Sophie Debrock, Jason M. Mwenda, and Thomas M. D'Hooghe. 2003. "Potential Involvement of the Immune System in the Development of Endometriosis." *Reproductive Biology and Endocrinology* 1.
- [22] Miller, Jessica E. et al. 2017. "Interleukin-33 Modulates Inflammation in Endometriosis." *Scientific Reports* 7 (1): 17903.
- [23] Moradi, Maryam et al. 2014. "Impact of Endometriosis on Women's Lives: A Qualitative Study." *BMC Women's Health* 14 (1): 123.
- [24] Murji, Ally et al. 2020a. "Use of Dienogest in Endometriosis: A Narrative Literature Review and Expert Commentary." *Current Medical Research and Opinion* 36 (5): 895–907.
- [25] P. V. Foti *et al.*, "Endometriosis: clinical features, MR imaging findings and pathologic correlation," *Insights into Imaging*, vol. 9, no. 2. pp. 149–172, 2018, doi: 10.1007/s13244-017-0591-0.
- [26] Riazi, Hedyeh et al. 2015. "Clinical Diagnosis of Pelvic Endometriosis: A Scoping Review." *BMC Women's Health* 15 (1): 01.
- [27] Rolla, Edgardo. 2019. "Endometriosis: Advances and Controversies in Classification, Pathogenesis, Diagnosis, and Treatment: [Version 1; Peer Review: 4 Approved]." *F1000Research* 8.
- [28] Saceanu, Sidonia Maria, Stefan Patrascu, Anca Patrascu, and Valeriu Surlin. 2017. "Endometriosis: When and How We Treat." In *Fertility-Oriented Female Reproductive Surgery*.
- [29] Shiges, Nina et al. 2019. "The Association between Endometriosis and Autoimmune Diseases: A Systematic Review and Meta-Analysis." *Human Reproduction Update* 25 (4): 486–503.
- [30] Zannoni, Letizia, Simona Del Forno, Roberto Paradisi, and Renato Seracchioli. 2016. "Endometriosis in Adolescence: Practical Rules for an Earlier Diagnosis." *Pediatric Annals* 45 (9): e332–35.
- [31] Zondervan, Krina T. et al. 2018. "Endometriosis." *Nature Reviews Disease Primers* 4 (1): 9.
- [32] S. Rai, Ashish, P. Kumari, A. Singh, and R. Singh, "Correlation of follicle-stimulating hormone receptor gene Asn 680 Ser (rs6166) polymorphism with female infertility," *J. Fam. Med. Prim. Care*, vol. 8, no. 10, p. 3356, 2019.