Best Practice & Research Clinical Obstetrics and Gynaecology
Vol. 22, No. 2, pp. 275–306, 2008
doi:10.1016/j.bpobgyn.2007.10.001
available online at http://www.sciencedirect.com

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Endometriosis: current and future medical therapies

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Endometriosis is a chronic inflammatory disease that responds to steroidal manipulation. Creation of a steady hormonal environment with inhibition of ovulation temporarily suppresses the ectopic implants and reduces the inflammatory status as well as the associated pain symptoms. Pharmacological management of endometriosis must be set within the framework of long-term therapeutic strategies. As the available drugs are not curative, treatments will need to be

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1521-6934/$ - see front matter

administered for years or until women desire a pregnancy. The various therapies studied have shown similar efficacy. Consequently, based on a more favourable profile in terms of safety, tolerability and cost, combined oral contraceptives and progestins should be considered as the first-line option, both as an alternative to surgery and as a postoperative adjuvant measure. Gonadotrophin-releasing hormone analogues, danazol and gestrinone should be used when progestins and oral contraceptives fail, are not tolerated or are contra-indicated. Future therapies for endometriosis must compare favourably with existing drugs before hypothesizing their implementation in current practice. Medical treatment is not indicated in women seeking conception because reproductive prognosis is not ameliorated.

Key words: endometriosis; pelvic pain; oral contraceptives; progestins; GnRH analogues; danazol; gestrinone.

THERAPEUTIC MANAGEMENT OF ENDOMETRIOSIS: A PROBLEM-ORIENTED APPROACH

For almost a century, the treatment of endometriosis has been based primarily on a straightforward oncological principle, i.e. radical removal of lesions. This is still a mainstay of therapy in cases of bowel and ureteral stenosis or adnexal masses with ultrasonographically doubtful characteristics. However, endometriosis is not a cancer and, in the vast majority of patients, it does not cause intestinal or ureteral strictures. Moreover, in the past two decades, it has become progressively evident that the overall 'amount' of disease is not correlated with frequency and severity of symptoms or with long-term prognosis in terms of conceptions and recurrences.[1] Accordingly, a more pragmatic approach to the treatment of endometriosis has developed, centred more on the woman's needs than on the extension of lesions.[2] In other words, the problems of patients with endometriosis are disease-related symptoms and not implants per se, and treatments should be focused on resolution of complaints, independently of a priori excision of lesions.

However, the two positions still co-exist and the debate continues. On one side, it has been stated that 'the definitive treatment of endometriosis is simple: surgical eradication' and that 'the success of surgical treatment is best assessed by determining how much disease, if any, remains after operative interventions'.[3] On the other hand, it has been considered that 'increasingly, the focus has been on using research outcomes that matter to patients' and that 'patient oriented outcomes of relief of pain and pregnancy rate […] are the outcomes considered to make a difference to the daily lives of women with endometriosis'.[4]

Medical therapy of endometriosis plays its role in this undefined clinical scenario. The purposes of the present review are to: discuss the general principles on which to base a pharmacological treatment strategy; describe the most frequently used types of drugs, analysing their efficacy and tolerability; and identify alternative hormonal as well as non-hormonal treatments under development that may become available in the future.

Only management of pain will be addressed, as it has been demonstrated repeatedly that medical therapy has no impact on fertility when given alone or as a postoperative adjuvant measure.[5–7] Indeed, 'more harm than good can be done by treatment, because of side effects and the lost opportunity to conceive'.[8] Conversely, the efficacy of hormonal drugs on endometriosis-associated algic symptoms has been proven by placebo-controlled randomized studies.[9–12]