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ENDOMETRIOZDA YUVENIL QON KETISHI BO'LGAN QIZLARNI DAVOLASH USULLARINI TAKOMILLASHTIRISH

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Abstract
Increasing evidence indicates that early-onset endometriosis (EE), beginning at menarche or early adolescence, may have an origin that is distinct from the adult variant resulting from neonatal uterine bleeding (NUB). This involves seeding naïve endometrial progenitor cells into the pelvic cavity; they can then become activated around thelarche. It can also be progressive, compromising future fertility. This variant appears to be characterized by the presence of an ovarian endometrioma. Today, the diagnosis of endometriosis in young patients is often delayed for years; with rapid progression, it can severely affect the pelvic organs even in the absence of serious symptoms. Given the predicament, much attention needs to be paid to symptomatology, which is often non-specific, justifying the search for new, simple, non-invasive markers of increased risk

Keywords: juvenile uterine bleeding, endometriosis, treatment of endometriosis

Introduction

Until recently, adolescent endometriosis was considered a rare, often transient condition, not particularly serious for younger patients. Against this background, and not without the disagreement of some, we have pointed out that early-onset endometriosis (EEE) can sometimes be severe, requiring rapid diagnosis and proper treatment.Brosens et al., 2013b, 2014). To support this view, we carefully reviewed published studies, including some early paediatric studies, and identified peritoneal reflux due to neonatal uterine bleeding (NMC), occurring in 3-5% of female newborns, as a biologically plausible and probable cause of EOE.Brosens & Benaggiano, 2013, 2016; Brosens et al., 2013a; Gargett et al., 2014).

Thus, at least some forms of adolescent endometriosis may represent a subtype of the disease that is different from that of adults.Brosens et al., 2016) that require special management. A review of recently published studies suggests that in the largest study ever published, EOE can be severe and progressive, especially in the form of ovarian endometrioma.Brosens et al., 2013b).

Clinical Presentation

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Marsh & Laufer (2005) described endometriosis as the cause of chronic pelvic pain in five girls in premenarche without obstructive abnormality of the reproductive tract. Laparoscopy identified and removed multiple clear and red lesions consistent with peritoneal endometriosis. Six and eight years later, two of the girls underwent repeated laparoscopy, documenting the reappearance of typical lesions. Subsequently, an 11-year-old girl in the premenarch was described as premenarcheal endometriosis with ovarian endometrioma or thin endometriosis. Gogach et al., 2012) and a 9-year-old girl (Ebert et al., 2009). It is estimated that the younger the girls at the time of diagnosis, the more severe the stage and size of the lesions. Emmert and Riedel, 1998), and that pelvic abnormalities, such as endometriosis or uterine abnormalities, can be found in about 10% of adolescents with severe symptoms of dysmenorrhea. Harel, 2008). Adolescents with chronic pelvic pain who do not respond to medication have been found to have a high incidence of stage I or II endometriosis.Laufer et al1997).

In adolescents, ovarian endometriosis caused by intussusception of the cortical layer of the ovaries, with or without adhesions, is of particular concern.

However, in clinical practice, the delay in diagnosis remains a serious problem; Especially taking into account the observation that the earlier dysmenorrhea appears, the longer the delay in diagnosis.Balweg, 2004; Shuddelist et al., 2012).

In the course of an investigation specifically aimed at teenagers,Tandoi et al. (2011)followed by 57 women aged 21 years and under for 5 years. 32 (56%) had a recurrence of the disease after surgery. Its frequency increased over time after surgery, with no obvious association with the location or stage of the disease, the type of surgery, and postoperative treatment. Recurrence was confirmed by repeated laparoscopy in 11 cases (34%), while in the remaining 21 cases (66%) it was assumed due to the recurrence of symptoms or based on clinical or sonographic data. Caution must be exercised in evaluating these results, as patients with appropriate follow-up are usually a select group and may not be representative of the general population.

Clinical conditions associated with an increased risk of neonatal uterine bleeding.

We have already considered a number of factors that can increase the incidence of NMP, and the likelihood of an association of these factors with the presence of EOE in adolescence. Brosens and Benaggiano, 2015). For this reason, they will be summarized here. Low birth weight and preeclampsia.

In the clinical series by Levy et al. (1964), low birth weight was reported to be the main cause of NUB, although no distinction was made between prematurity and low birth weight for gestational age. Another important association with NUB was the presence of preeclampsia. The risk increased to 32% for mild preeclampsia and up to 46% for severe form.

After ripening. In the study Levy et al. (1964)The risk of NUB in post-adulthood was also increased, albeit slightly. In a cohort study Beric' and others. (1985), 126 babies were premature, 2241 full-term and 110 post-term. The incidence of NUB was 0.78%, 3.79%, and 9.10%, respectively, confirming that prematurity is an important cause. Feto-maternal incompatibility. Levy et al. (1964) found an increased risk of NUB due to ABO blood group incompatibility or Rh at term. The risk was very significant.

Epidemiological links

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Several epidemiological studies have investigated the association between intrauterine events and the risk of endometriosis.

Missmer et al. (2004)documented increased risk of endometriosis at lower birth weight with a relative risk of 1.2 (95% CI 1.0 to 1.8; P <0,01). In the Nurses' Health Study II with a 10-year follow-up, after adjusting for age, calendar time, parity, race, and body mass index, there was a linear increase in the incidence of endometriosis at age 18 with a decrease in birth weight (RR 1.3 for birth weight ≤ 5.5 pounds compared to 7.0 to 8.4 pounds, 95% CI 1.0 to 1.8, P = 0,01). Preterm birth was not associated with an increased risk of endometriosis. Vitonis et al., 2010). Patients with a birth weight of 2500 g or less had a higher risk of endometriosis. A "dose-dependent effect" was observed for risk based on birth weight, as well as an increased risk of developing profound infiltrative endometriosis. In contrast, another smaller case-control study that involved 91 women with endometriosis and 82 women from the control group.Somillana et al. (2011) No association with prematurity or birth weight could be found

To determine disease progression through interstitial fibrosis and microvascular damage associated with endometrioid ovarian cysts, Qiu et al. (2012) Used transvaginal color Doppler and evaluated interstitial ovarian blood flow, finding that changes in resistance indices in the ovaries with endometriosis were associated with interstitial fibrosis and devascularization.

The question is complex and recently Kelleher & Goldstein (2015)It was pointed out that in order to conduct a proper differential diagnosis of tumors of the appendages in childhood, the pediatrician needs to be well aware of the wide range of pathology of the appendages.

Medical Treatment

In a paper prepared under the auspices of the World Endometriosis Society (Johnson & Hummelschoy, 2013), the consensus was that in the treatment of EOE, both medical and surgical techniques can improve quality of life, relieve symptoms, prevent the development of more severe disease later in life, and minimize the likelihood that future fertility may decline. Compromised.

In principle, the same drugs can be used in adolescents and adult patients. However, a critical issue is the mentioned progressive and dynamic nature of endometriosis, which manifests itself in both spontaneous and induced disease.D'Houge et al., 1996; Harirchyan et al., 2012; Zhang et al., 2016a, 2016b, 2016c).

In a mini-review of dysmenorrhea in adolescence, Harel (2006)states: "If dysmenorrhea does not improve within 6 months of treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and oral birth control pills, laparoscopy is indicated to detect endometriosis." Estrogen-progestin combinations have been empirically used to treat young patients with suspected or confirmed endometriosis, sometimes with good results. Doctors are reluctant to use GnRH analogues, especially in young patients, due to secondary hypoestrogenic side effects; However, so-called "addition" therapy may be a means of overcoming this problem.

Combined surgical and medical approach

In its review of treatment options for adolescent endometriosis,Laufer et al. (2003), argue that the goal of treatment is twofold: to treat pain that may persist in the case of suboptimal ablation and to slow the progression of the disease.

Thus, it seems that the correct treatment of adolescents should consist in prescribing medications after minimally invasive surgery. In this context, a study involving 194 adolescent and young adult

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women found that postoperative administration of norethisterone acetate is an effective treatment option for pain and bleeding in all stages of endometriosis.Kaser et al., 2012).

New options

There is palpable frustration over the slow progress in the development of new therapeutics, and several new drugs have been approved over the past decade to treat endometriosis.Vercellini et al., 2011).

At the same time, several experimental drugs have undergone preliminary evaluation and seem to have shown promising results.

One option is to use dopamine receptor agonists (ADRs), compounds capable of activating signaling pathways leading to changes in gene transcription.Delgado-Rosas et al., 2011; Novella-Maestre et al., 2009.). In a small clinical study, the administration of quinagolid DRA in patients with hyperprolactinemia led to a decrease in peritoneal endometrioid foci in two-thirds of cases, and to elimination in a residual third (Gomez et al., 2011.). Histologically, degeneration was confirmed by suppression of vascular endothelial growth factor (VEGF) and its receptor-2 (VEGFR2), three proangiogenic cytokines, and a plasminogen activator-1 inhibitor (PAR-1). In this study, ADRs reduced inflammation, affected angiogenesis, and enhanced fibrinolysis.

For both ADR and valproic acid, large clinical trials have never been conducted. Given that these are old drugs and their patents have long expired, it is unlikely that any large-scale clinical trials will begin anytime soon.

Medical and surgical treatment can cause long-term concerns, although reliable data are still lacking.

Adolescent girls and young women are in the final stages of their development and are ready to realize their reproductive potential.

Since most, if not all, drugs are hormonal, some concerns have been raised about their long-term effects, given that many tissues and organs express estrogen and progesterone receptors. It is known that in female rodents, estradiol and progesterone regulate sexual behavior, ranging from readiness for mating, arousing the interest of the male partner and ending with successful copulation.Erskine 1989; Pfaus et al., 1999; Sakuma, 2008). When taking large doses of estradiol, repeated priming with estradiol, or in both cases, the susceptibility of female rodents can manifest itself even without priming with progesterone.Jones et al., 2013; Micevich et al., 2008; Parsons et al., 1984; Pfaff et al., 2002; Uphouse et al., 2014). Even taking into account the significant differences in humans, any hypoestrogenic environment resulting from treatment could theoretically lead to long-term effects far beyond those related to bone mineral content.

Inference

The aim of this review was to critically reassess current early-onset endometriosis treatment, starting with its possible non-adult origin and new knowledge about its symptomatology and pathogenesis, continuing with the search for new, simple, non-invasive high-risk markers, and ending with a reassessment of the usefulness of new imaging screening methods.

In extraovarian endometriosis, the main problem is associated with the almost inevitable delay in its diagnosis. This is due, on the one hand, to the often nonspecific symptoms in adolescence, and on the other, to the reluctance of gynecologists to use currently available invasive diagnostic techniques. For this reason, the wider use of new non-invasive techniques of transvaginal

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ultrasound and MRI in adolescence to detect the presence of all forms of endometriosis is mandatory.

Diagnosis of mild endometriosis in adolescents by transvaginal ultrasound is still limited to a relatively small number of specially trained specialists; Various MRI techniques seem to be able to detect the presence of endometriosis in its various forms in most young patients.

We suggest that in the presence of pelvic pain, dysmenorrhea, and ovarian cystic structure visible on transvaginal ultrasound or MRI, feto-maternal factors that increase the risk of neonatal uterine bleeding can be used to focus attention on higher-risk cases, such as in women with endometriosis. of neonatal origin. This will reduce the current delay in time until diagnosis. Indeed, fetomaternal factors, including preeclampsia and fetal growth retardation, have a common presence of uteroplacental disorders with a decrease in the blood supply to the placenta, whereas a history of fetomaternal incompatibility may indicate the presence of chronic fetal anemia. All of these conditions cause fetal hypoxia and distress in the last months of pregnancy. The identification of abnormalities associated with uteroplacental ischemia, such as preeclampsia and fetal growth retardation, should be used to make a potential distinction between endometriosis of neonatal and adult origin. All this, however, can only be achieved with properly designed prospective studies.

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