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PATIENT PERSPECTIVE

Endometriosis, an everlasting challenge

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Endometriosis is one of the most common benign gynecological diseases affecting 5-10 % of women of fertile age, and the condition has received much attention. In spite of this, there are still challenges concerning diagnosing and treatment. The diagnostic delay can be more than ten years, and is especially long concerning teenagers. The symptoms can start already in adolescence, but this knowledge has not fully reached out to the medical profession, for example to general practitioners and pediatricians. As no hormonal treatment has proved to be superior, the least complicated drugs such as combined oral contraceptives or progestins should be the first choice for control of pain. Endometriosis is associated with infertility and in this respect hormone treatment has no role and will only further delay the chance to conceive, whereas in vitro fertilisation (IVF)

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is mostly successful. Proper information about endometriosis to the public and medical profession is a challenge.

- Adolescents should be informed about unacceptable menstruations
- General practitioners and pediatricians should be familiar with the symptoms of endometriosis
- Oral combined contraceptives or progestins are first choice for pharmaceutical treatment
- Balanced information to patients and in the media is needed

Endometriosis is a common disease, affecting 5-10 % of women of fertile age (1), and it has been estimated that 176 million women worldwide are affected by endometriosis (2). It is thus one of the most common gynecological diseases in women of fertile age. Endometriosis has been intensively investigated with more than one thousand articles presented annually, a publication rate that has doubled within the last decade (3). Recurrent international and national congresses, workshops and meetings are arranged only to discuss this condition. Endometriosis societies have been founded, international and national guidelines are prepared. with regular updating. Patient associations exist all over the world. An endometriosis awareness month takes place across the globe during the month of March with a mission to raise attention to the disease (2).

In spite of this apparently massive interest in endometriosis, there are still many frustrations among the patients as well as challenges for professionals concerning patient care. I here want to focus on some issues I find important for patients and for the medical profession.

The diagnostic delay

From a patient's perspective, the delay in getting the diagnosis is of major concern. The time from appearance of symptoms to a definitive diagnosis is from five years to more than 12 years. Even with increasing awareness of endometriosis, the diagnostic delay has not been shown to be shortened (4, 5).

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The delay is primarily a 'patient's delay', probably a reluctance to seek medical help. Young age significantly increases the delay of diagnosing endometriosis (6), and quite often the first signs of endometriosis have their debut in teenagers shortly after the menarche. However, the parents of the young girl may consider painful menstruations to be a normal pattern or misinterpret the symptoms as refusal to go to school. The consequences may be reduced school performance, social isolation and a poor self-esteem in a vulnerable period of a young woman's life. It is important to inform about the menstrual symptoms which should be considered abnormal such as cramps not responding to either painkillers and NSAIDs or cyclic oral contraceptives. A program on Menstrual Health and Endometriosis has been developed in New Zealand to approach pupils in secondary school (7). A similar educational program could be adapted and widely included in the school curriculum. Educators should participate in this process as they know how best to approach adolescents.

The next step on the trail to diagnosing endometriosis is a consultation with a general practitioner or a pediatrician. Are they prepared to understand and interpret the symptoms? Are they aware of endometriosis as a differential diagnosis? If not so, this will add one more delay, the 'doctor's delay'. So far, most textbooks in pediatrics do not mention endometriosis at all, and societies for pain in children do not include links to endometriosis on their homepage. Previously even overview articles hardly or not at all mentioned endometriosis as a differential diagnosis for pelvic pain in adolescents (8, 9). There are now promising movements towards creating greater awareness about endometriosis among pediatricians with practical rules for managing adolescents with dysmenorrhea and chronic pelvic pain (10, 11).

It is debated whether an early diagnosis in adolescents is important for control of endometriosis and for preservation of fertility. Case reports of adolescents left with untreated endometriosis have shown deterioration, and close follow-up is therefore recommended (12). However, a synopsis of randomised studies with placebo or an untreated arm disclosed that there was almost equal chance for endometriosis to disappear, to be stable or to worsen (13).

Labelling a young woman with a chronic sickness is a double-edged sword. On the one side, she has a cause and a name for her condition and thus an accepted explanation for her symptoms. The patients themselves request an early diagnosis to get appropriate medical care and social acceptance for their sickness with periodical incapacity. On the other side, having a disease known to comprise multiple symptoms may become a hindrance for unveiling alternative causes. In addition, awareness of possible outcomes of endometriosis

such as infertility, dyspareunia and repeated surgery could add an extra burden to her life. A compromise could be to postpone laparoscopy and offer empiric treatment with hormones such as continuous estrogen/progestin or progestin as proposed in the Canadian guidelines (14). One cannot ignore that probably many young women are adequately treated for endometriosis without ever having their diagnosis verified.

Most women get the first signs of the disease when they are in their twenties (4). Pain symptoms such as dysmenorrhoea, dyspareunia, dysuria and dyschezia should be a clue to diagnosis for the general practitioner, especially if the symptoms are cyclic and combined with subfertility (6). It has, however, been estimated in the Netherlands that general practitioners annually meet on average 2.8 women which they could suspect of having endometriosis. With this uncommonness the physicians do not easily identify that the symptoms could be caused by endometriosis (15). Endometriosis should be entitled to have a central place in the gynecological curriculum for medical students and in the continuing education in primary health care.

Hormonal treatment

After having obtained the diagnosis, probably in combination with surgery, the next challenge is to select an appropriate hormonal treatment. Far too often gonadotropin-releasing hormone (GnRH)-agonists are chosen because they by many colleagues unwarranted are considered to be the 'drug of choice' in endometriosis as the most potent treatment. A recent unpublished survey among Norwegian gynecologists disclosed that by one third, GnRH-agonists were considered to be the most effective hormonal treatment for endometriosis. However, no hormone has proved to be superior to any other in the therapeutic armamentarium consisting of combined oral contraceptives, progestins (as tablets, depot-injections or intrauterine system), danazol and GnRH-agonists (16, 17). So why not start with continuous combined oral contraceptives or progestins as they are well accepted and cheap drugs?

New hormones are studied in non-inferiority trials such as for example the progestin dienogest tested against leuprolide acetate (18), and not against older and inexpensive progestins. Most studies on new drugs are of a short duration and do not reflect the reality that women often need to be treated for years. Since it is a benign disease, treatment of endometriosis should not be more troublesome than the disease itself. Patients may get a

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prescription and a new appointment after maybe half a year, but the women deserve a close follow-up with possible adjustment of dose and 'add-back' therapy to counteract side effects. Personally, I prefer checks every three months, and in some cases it can be arranged as telephone calls. These contacts could probably be organized by a trained nurse, a routine used for other chronic disease such as diabetes and multiple sclerosis. In clinical trials there is a schedule for regular follow-up, this could modified for our daily practice.

If a treatment fails to relieve pain despite of apparent effectiveness in suppressing menstrual periods, it is important is to consider whether endometriosis may not be the real cause. Women should not continue hormonal treatment over a long period if it does not work. Referral to a multi-disciplinary pain team should be the next step.

It should be kept in mind that a suspicion of endometriosis could in some cases be a sidetrack or a pretext for not exploring the true cause of the symptoms. Endometriosis can also be an incidental finding without clinical relevance and without risk of aggravation (19). Personally, I recall a patient diagnosed with endometriosis who at that time received danazol with minor efficacy, but severe side-effects, for a long time until she developed iridocyclitis. Ankylosing spondylitis turned out to be the correct diagnosis.

Infertility

Subfertility is common in endometriosis and this is a burden added to the physical pain. Patients should be encouraged and told that the majority of women with endometriosis have normal or close to normal fecundity. It has for decades been determined that medical treatment does not increase the fertility rate, whereas laparoscopic surgery may improve pregnancy rates (16, 20). The coexistence of pain and infertility is a therapeutically challenge as hormonal treatment for pain acts also as a contraceptive. A close contact between general gynecologists and infertility centers are desirable for developing a treatment plan that takes into account the patient's needs.

IVF is an effective way to obtain pregnancy in the presence of endometriosis, as the success rate is almost as high as for tubal infertility (21, 22). A retrospective Norwegian study showed that 75% of women with endometriosis and infertility obtained a biological child, either spontaneously or by assisted reproduction (23). As we cannot predict the development of endometriosis, the patients should be advised not to postpone attempts to

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become pregnant unnecessarily, also because age is an important factor for successful reproduction..

Information and media

When informed of the diagnosis, - whether suspected or confirmed - it is frequently the first time the patient hears the word "endometriosis". This generates distress and anxiety. Knowing this is an abnormal growth means associations with cancer. Repeated verbal information from health providers is essential and should be combined with written information. The internet is an enormous source of information with more than eight million hits just for 'endometriosis', but with a quality which ranges from excellent down to confusing and erroneous. Health professionals should warn about the risk of outdated and inaccurate information online which could delay proper treatment, could be expensive and even dangerous. The patient associations have a great responsibility to spread balanced and well documented material about the disease, and dedicated gynecologists should join this process.

We who are professionally engaged in endometriosis are often contacted by journalists who have heard about this 'mysterious' disease and want to make an article or a program. This is a golden opportunity to spread information, but often this event leads to a struggle with the journalist and the patient societies who want to present the worst cases to show the seriousness of the disease and associate it with incapacitation and hopelessness (24, 25). The media in this way give a skewed and unbalanced description of outcomes and overlook treatment possibilities for pain management and fertility (23). Medical experts on endometriosis and patient groups should work together to disseminate the most updated and nuanced knowledge about endometriosis to the medical profession and to budgetary authorities so the patients can receive the best support for their chronic disease.

Conclusions

Endometriosis affects 5-10 percent of women of fertile age and symptoms can start already in teenagers. There is a considerable diagnostic delay in diagnosing the disease, especially in young patients. Continuous combined oral contraceptives or progestins should be a first treatment choice. Hormones do not improve fertility, but IVF is often successful. Information

about typical signs of endometriosis should be given to adolescents, to the population in general and to health care providers at all levels of care.

Conflicts of interest:

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