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Current Treatment Approaches of Uterine Fibroids

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Abstract

Myoma uteri are the most common benign uterine tumors among women of reproductive age . These benign tumors are a public health problem worldwide. There are many options for the treatment of uterine myoma. Place in medical treatment of uterine myoma treatment is limited due to side effects and drug costs. Medical treatment is usually used temporary in the form of before surgery. Surgical treatment of uterine myoma should be individualized according to patient age, size and location of myoma. Treatment with interventional radiological methods of uterine myoma is not common for the moment. Such as the lack of risk associated with surgery, shorter time to return to normal life is advantages of interventional radiological methods.

Keywords: Myoma uteri, fibroids, treatment

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Introduction

Uterine fibroids (leiomyomas) are benign tumors arising from the myometrium. Among women of reproductive age are the most common uterine tumor with 20-25% [1]. The fibroids are are diagnosed during a pelvic examination and confirmed by ultrasound. Pelvic pain, dysmenorrhea, menorrhagia, pelvic pressure are the most common symptoms of fibroids.

Asymptomatic fibroids may be followed unattended [2]. Updated guidelines also supports the expectant managment of asemptomatic fibroids [3-5].

Timing and type of intervention should be indivudialized according to the age of patients, severity of symptoms, size and location of fibroids [6].

Medical Therapy

There is no optimal medical treatment resulting in cure of fibroids. Medical treatment is usually used temporary in the form of before surgery. Medical therapy provides adequate symptom relief in some women, primarily in situations where bleeding is the dominant or only symptom. The majority of women get some improvement over one year of therapy, but long-term failure rates are high [7]. In the study published in 2006 observed that 60% of patients went to surgery in 2 years [8].

A -Hormonal therapies

Estrogen-progestin contraceptives

Previously Estrogen-progestin contraceptives (COC)'s was considered to be a risk factor in the growth of fibroids. But now many meta-analysis of studies observing that using COCs are associated with a decreased risk of fibroids and reduced symptoms [9]. Therapeutic studies suggest that it may be effective before invasive procedures. The mechanism of reduce bleeding of the drug is associated with creating endometrial atrophy.

Oral and injectable progestogens:

Progesterone reduces bleeding by causing endometrial atrophy. This group of drugs evaluated in patients with mild to moderate symptoms and prompt contraception. Studies observed that

these agents are associated with a decreased risk of leiomyoma formation [10,11]. Sudden bleeding, breast tenderness, weight gain, decreased libido, and depression are side effects of this treatmen reduce treatment.

Levonorgestrel-releasing intrauterine system (LNG-IUS) :

The Levonorgestrel-releasing intrauterine system (LNG-IUS) was introduced as a contraceptive device. LNG-IUS can provide a good reduction in menorrhagia, but its effect on the size of uterine fibroids is still being debated [12,13]. A prospective study comparing the efficacy of the LNG-IUS in improving anormal uterine bleeding two groups of women, with and without fibroids, has demonstrated an 86% decrease in bleeding intensity in both groups. After 4 years, there was a 99.5% decrease in both groups and also a reduction in uterine volume in the group with fibroids [14]. Another study reported that 64% of women who used the LNG-IUS canceled their plans to undergo a hysterectomy within a 6-month period of the study [15].

Patient should be informed about the general characteristics and side effects (oligomenore amenore) of LNG-IUS. The manufacturer states that the use of the LNG-IUS is contraindicated with congenital or acquired uterine anomaly including fibroids if they distort the uterine cavity.

Gonadotropin-releasing hormone agonists:

Gonadotropin-releasing hormone (GnRH) agonists are the most effective medical treatment option for uterine myoma. These molecules induce a state of hypoestrogenism due to inhibition of the gonadal axis, with consequent hypogonadism. Initially, they increase gonadotropin secretion (flare up effect, but after competing with the GnRH molecule, they cause a down-regulation of GnRH receptors. Another important mechanism is a decrease of several important mediator (Insulin-like growth factor 1, epidermal growth factor and transforming growth factor-beta) of fibroid growth [16].

Most women will develop amenorrhea, improvement in anemia, and a significant reduction (aproximately 50 percent) in uterine size within three months of initiating this therapy. Preoperative treatment of GnRH agonist use, a reduction in operative time, blood loss, and causes a reduction in length of hospital stay.

The disadvantages of GnRHa include cost, syptoms of menopause (hot flashes, vaginal dryness, sleep disturbance), and with prolonged therapy, bone demineralization. GnRHa cannot be used as long-term standalone therapies for fibroid disease because of the rapid rebound growth of the fibroids upon cessation of therapy [17].

Gonadotropin-releasing hormone antagonists:

The clinical effects of GnRH antagonist are similar to agonists. The advantage of this agents is the rapid onset of clinical effects without the characteristic initial flare-up observed with GnRH agonist treatment.

B- Progesterone receptor modulators

Ulipristal acetate(UA):

Ullipristal acetate (UA) is a a progesterone receptor modulator which inhibits ovulation. It is associated with a reduction in pain, bleeding, and leiomyoma size between 17% and 24% [18] as well as an improvement in quality of life [19].

A randomise study which compared UA and GnRHa, observed that resolution of menorrhagia was achieved more quickly in the ulipristal groups Women treated with ulipristal had a significantly lower frequency of moderate to severe hot flashes. The reduction in uterine size was significantly lower for the ulipristal groups[20].

Mifepristone:

It has recently been evaluated as a potential therapeutic agent for uterine leiomyomas with a dose that ranges from 5 mg to 50 mg over a 3-month period [21]. Daily administration of mifepristone 5 mg and 10 mg has shown uterine volume reductions of 48% after 6 months and 52% after 1 year, for both doses [22].

In 70% of patients using the mifepristone is also developing within 1 year of amenorrhea [22]. Use of high doses has been reported that serum aminotransferase raise. However, in the low-dose regimen it is very rare [23].

C-Selective Estrogen Receptor Modulators:

Raloxifene:

The efficacy of selective estrogen receptor modulators for treatment of leiomyomas is unclear. Raloxifene has been showed to enhance the shrinkage of uterine leiomyomas in postmenopausal women [24]. However, a recent report from Italy that addressed the effect of raloxifene on uterine leiomyomas showed that the leiomyoma size in premenopausal women who were administered raloxifene over a 2-year period exhibited no change in leiomyoma size [25].

D- Aromatase inhibitors:

Aromatase inhibitors significantly block both ovarian and peripheral estrogen production within 1 day of treatment [3]. One randomized clinical trial have described shrinkage of symptomatic leiomyomas and a decrease in leiomyoma symptoms in women given aromatase inhibitors [26].

E-Nonsteroidal antiinflammatory drugs:

There are not enough studies on the effects of menorrhagia associated with leiomyoma. Nonsteroidal antiinflammatory drugs do not appear to reduce blood loss in women with myomas, but they act by reducing dysmenorrhea [27,28].

F-Androgenic Agents:

Danazol and gestrinone:

Androgenic steroids are effective in the treatment of leiomyoma symptoms. Danazol is correct anemia caused by fibroids are related with menorrhagia but does not reduce fibroid uterine volume.

Side effects (weight gain, muscle cramps, reduction of breast size, acne, hirsutism, such as increased liver enzymes) are often seen and they are limiting for the treatment.

Surgery

Surgery is the main treatment modality of fibroids. Fibroids represent one of the most frequent indications for major surgery in pre-menopausal women and , they constitute a public health problem [29].

Hysterectomy:

Hysterectomy is the definitive procedure and fibroids are the most common reasons for hysterectomy [30]. Hysterectomy is preferred in acute hemorrhage unresponsive to other treatments, women who have completed childbearing.

Morbidity of hysterectomy may outweigh the benefits at subserosal fibroids, stalked fibroids, submucosal fibroids. In these cases evaluated laparoscopy or hysteroscopy for treatment [31]. Avoiding the morbidity of hysterectomy should also be considered by patient whose only symptom is bleeding, or who are in the perimenopausal period; these women are often effectively treated with either a levonorgestrel-releasing IUS or endometrial ablation.

Myomectomy:

Myomectomy is an effective treatment option women who have not completed their fertility and who wish to retain their uterus. However, the disadvantage of this procedure is risk of recurrent fibroids.

Although the classical approach is laparotomy, laparoscopic and robotic-assisted procedures are becoming more common. Hysteroscopic myomectomy is appropriate procedures at the submucous myoma.

Endometrial ablation:

Hysteroscopic myomectomy alone or in combination can be used in women who have completed childbearing.

Myolysis:

Myolysis (i.e., delivering energy to tumors to desiccate them directly or disrupt their blood supply) is most often performed with the laser or bipolar needles. Combination treatment with

myolysis and endometrial ablation may reduce the need for subsequent procedures in patients with persistent bleeding [32].

Myolizis is easy but localized tissue destruction without repair may increase the chance of subsequent adhesion formation or rupture during pregnancy [33].

Uterine artery occlusion:

Altough experience is limited, Occlusion of uterine vessels either via laparoscopy or a vaginally-placed clamp has been proposed as an alternative to uterine artery embolization [34].

Interventional Radiology

Uterine artery embolization:

Uterine artery embolization (UAE) using embolic particles to occlude the uterine arteries, have been reported as a relatively safe, effective, and can be nonsurgical alternative to hysterectomy in diminishing fibroid. UAE performed by an experienced interventional radiologist.

UAE results in shrinkage of myomas of approximately 30 to 46 percent [35]. UAE have a shortened hospital stay, less pain than following surgery and a quicker return to work than those undergoing surgery [35,36].

Magnetic resonance guided focused ultrasound:

Magnetic resonance guided focused ultrasound is a more recent option for the treatment of uterine leiomyomas in women who have completed childbearing and treatment option for women with symptomatic uterine fibroids unresponsive to medical treatment. This noninvasive technique generates localized high temperature in the selected area and coagulates chosen tissue, leaving the skin and tissues in between unharmed [37-39].

This system is not indicated for leiomyomas which are resectable with a hysteroscope, heavily calcified, or when intervening bowel or bladder could be damaged by treatment.

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