UTERINE FIBROIDS: AN INTEGRATIVE APPROACH

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INTRODUCTION

Uterine fibroids are estimated to be present in 20–40% of reproductive age women, indicating that they are the most common gynecologic pelvic neoplasm. The term “fibroid” is really a misnomer because this tumor consists largely of smooth muscle rather than fibrous tissue, and is thus more appropriately termed “leiomyoma.” Leiomyomas are usually asymptomatic and benign. Women of African descent are 3–9 times more likely to have these tumors. They are not identifiable before puberty and normally grow only during the reproductive years, sometimes achieving significant proportions that can result in symptoms of increased pressure on the pelvic structures. Additional symptoms can include abnormal endometrial bleeding, infertility and spontaneous abortion. Fibroids, when present, are usually multiple and can attain huge proportions, weighing as much as 100 pounds. Malignant transformation is rare, accounting for less than .5% of tumors; however, excessive bleeding is common and often results in hysterectomy when blood loss is severe.

DISCUSSION

Pathogenesis

The cause of uterine fibroids is unknown, but research has demonstrated that estrogen receptors are present in higher concentrations than the surrounding myometrium. Estrogen therapy has also been known to cause sudden increases in their size. Conversely, low levels of estrogen such as seen with menopause will often result in their disappearance. While there is no definitive evidence that estrogen causes leiomyomas, this hormone is certainly implicated in fibroid growth and this knowledge provides rationale for effective treatment.

Fibroid Classification

Leiomyomas are usually multiple, discrete, and spherical with a clear demarcation from surrounding tissue. They consist of varying amounts of smooth muscle and fibrous connective tissue.

Fibroids originate in the myometrium, the muscular portion of the uterus, and are classified according to anatomic location.

Subserous fibroids lie on the outside of the uterus and are usually pedunculated, meaning they are attached via a stalk-like projection. Intramural fibroids grow within the uterine wall, giving the uterus a variable shape. Finally, submucous leiomyomas lie just beneath the endometrium and can bulge into the lumen, or cavity of the uterus as they enlarge. Occasionally, a submucous tumor will become pedunculated and exit partially through the cervix to create a “pedunculated vaginal fibroid”.

Clinical Findings

Symptoms: About 35–50% of women with fibroids will experience symptoms that are generally consistent with size and location. However, even very large masses may not produce any complaints, while a small fibroid in the “wrong” place may be debilitating.

1. **Infertility:** About 2–10% of patients with fibroids will experience an inability to conceive. The cause of infertility is thought to be abnormal tubal or uterine motility, interference with sperm movement, or abnormal blood flow.
2. **Pressure Effects:** Depending upon their location, leiomyomas can compress or obstruct several structures. The most common complaint is urinary urgency and increased frequency due to pressure upon the bladder. With very large tumors patients may experience constipation and lower extremity edema secondary to pelvic venous congestion.
3. **Abnormal Endometrial Bleeding:** Abnormal uterine bleeding is the most common symptom associated with fibroids and is present in about 30% of patients. Women suffering with fibroids will characteristically have a heavy, prolonged menstrual flow (menorrhagia). Premenstrual spotting is common, as is light flow following menses. Additionally, some women will have varying degrees of metrorrhagia (intermenstrual bleeding). When severe, these abnormalities in menstrual flow can cause chronic blood loss with resulting iron deficiency anemia or even hypovolemia. These conditions can be life-threatening and necessitate aggressive medical intervention if not controlled.

4. **Pain:** Pain is not a typical symptom ascribed to leiomyomas. When present, it is usually due to degeneration within a tumor after circulatory occlusion, infection, or torsion of a pedunculated fibroid. Occasionally a tumor will compress nerves against the bony pelvis and result in radiating pain.

Conventional Treatment

Most women with uterine leiomyomas do not seek treatment. For severe bleeding blood transfusions are sometimes necessary. Otherwise, conventional treatment depends upon a patient's age, desire to have children, general health, the size and location of the fibroids, and the severity of symptoms.

1. **Hormone:** For excessive or unusual bleeding, oral contraceptives are sometimes employed in an attempt to regulate menstruation. Although this method is sometimes effective to halt excessive blood loss, this intervention does nothing to address the fibroids themselves. In contrast, Luteinizing Hormone Releasing Hormone (LHRH) analogues such as Lupron® are used to shut down endogenous estrogen and progesterone production. Although a cessation of estrogen synthesis may prevent further growth of a fibroid, this chemically induced menopause results in a host of undesirable symptoms that include hot flashes, loss of libido, breast shrinkage, and vaginal dryness.
2. **Dilatation and Curettage (D&C):** A D&C is usually performed when excessive uterine bleeding is not controlled with oral contraceptives. The procedure is both diagnostic—in that pathology can be performed on obtained tissue—and therapeutic, in that sometimes metrorrhagia and menorrhagia will be ameliorated. A D&C is not used for sizable tumors and is not an option to manage fibroids themselves.
3. **Myomectomy:** Myomectomy, or removal of the fibroid itself, is indicated for women with significant symptoms who wish to preserve fertility. Patients who are candidates for this surgery are also restricted by the size and location of the mass. Unfortunately, even when the procedure is successful, it is not unusual for new fibroids to grow back.
4. **Hysterectomy:** A surgical removal of the uterus is performed when a patient's life is in danger due to excessive bleeding, pressure symptoms are severe, or the fibroid is so large that removal is aesthetically desirable.

Unfortunately, countless women have undergone varying degrees of conventional treatment intervention—many suffering hysterectomies—having been denied

the option of alternatives offered by natural medicine and other alternative therapies.

An Integrative Approach

Although there are few studies exploring the efficacy of the alternatives about to be described, fibroid therapy should be attempted with a judicious continuum of most conservative, non-invasive treatments first; followed by increasingly heroic measures ending if necessary, with the irreversible finality of hysterectomy. This insures that procedures carrying significant risk are not performed until less risky interventions have failed. However, far too many of us delivering alternative therapies experience the antithesis of this medical prudence. Patients often seek us out as a “last resort,” after have suffered the “slash and burn” mentality that is the cornerstone of mainstream medicine.

Uterine fibroids are difficult to treat. It is my approach to combine everything and anything that has reasonable therapeutic justification with minimal negative consequences. Satisfactory results are usually dependent upon patient compliance that necessitates strict dietary modifications, adherence to supplement and herbal prescriptions, as well as a commitment to behavior modifications.

1. **Dietary Modifications:** Because of the apparent relationship between estrogens and fibroid growth, dietary recommendations consist of minimizing the oral intake of synthetic estrogens, eating foods shown to facilitate estrogen biotransformation, increasing dietary fiber, and eating complex carbohydrates such as those found in vegetables and grains.
 - a) Ingestion of estrogenic compounds must be eliminated to prevent continued stimulation of leiomyomas. This consists of significantly reducing animal flesh intake and eating only free-range meats that are certified to be hormone free. Use of hormones in the meat and dairy industry is well documented. An October 1983 FDA report found that Synovex-S, an estradiol product that is given to livestock, increases estradiol concentrations in cattle by 12 fold. When cattle are slaughtered shortly following hormone implantation, levels are even higher (1). A November 1991 FDA report found that the concentration of the implant Revalor, containing estradiol and testosterone, to be as high as 50 parts per billion in beef liver (2). Sources of externally-derived estrogens are not limited to livestock. There are more than 20 man-made, estrogenic chemicals present in a wide variety of foods commonly eaten. Many are pesti-

cides, however, numerous are industrial pollutants, food additives, and packaging materials. Patients undergoing treatment for fibroids must make a reasonable effort to avoid these substances by eating only organic produce, drinking filtered water, and limiting the use of plastics for storage and re-heating of foods. Alternatives to oral contraceptives must also be explored due to the likelihood that the synthetic estrogen used in these drugs stimulates fibroid growth.

- b) The ultimate biologic effect of estrogen in the body depends predominately upon its metabolism and detoxification. Estrogen biotransformation occurs primarily in the liver via Phase I hydroxylation and Phase II methylation and glucuronidation pathways, which allow estrogen to be modified into a water-soluble, excretable compound. The initial phase of detoxification yields 3 estrogen metabolites that vary greatly in biologic activity: 2-hydroxyestrone (2-OH), 16- α -hydroxyestrone (16 α -OH), and 4-hydroxyestrone (4-OH) (3). The 2-OH is considered a "good" estrogen metabolite because it is very weak and may have beneficial effects in the body including the blocking of more potent estrogens. In contrast, the 4-OH and 16 α -OH have potent estrogenic activity and may promote the growth of estrogen sensitive tissue. (3,4) Dietary intake of cruciferous vegetables like broccoli and cabbage, as well as soy, can significantly increase the amount of 2-OH by modifying the activity of Phase 1 cytochrome P-450 enzymes.
- c) An increase in fiber intake promotes the excretion of estrogen by binding the hormone in the digestive tract. Soluble fiber, such as lignans found in flaxseeds, also increase sex hormone binding globulin (SHBG), thereby decreasing the amount of bioactive estrogen available to the tissues (5). Most estrogen is bound to SHBG rendering it inactive and therefore unable to exert estrogenic effects.
- d) A diet high in complex carbohydrates, such as whole grains and vegetables, helps stabilize blood sugar and insulin production that ultimately creates positive secondary effects on sex hormone balance (6).

A successful fibroid treatment plan thus includes the patient adopting a plant-based diet that is high in fresh, organic vegetables. Weight loss should be attempted in overweight individuals because high body fat results in high estrogen levels. Alcohol should also be avoided because it likewise results in elevated estrogen.

2. **Nutraceutical Supplementation:** Dietary modifications are an important element in the treatment of uterine leiomyomas; however, diet is insufficient as a stand-alone therapy. The supplementation of specific plant chemicals, vitamins, and minerals can further facilitate beneficial adjustments in the activity of estrogen and its several metabolites.

- a) Indole-3-carbinol is a naturally occurring compound derived from cruciferous vegetables, and like these plants, can increase the ratio of "good" 2-OH estrogen (7). As already explained, this "weaker" metabolite may bind to estrogen receptors in fibroids, thereby inhibiting the stimulating effects of more potent estrogens. The use of this over-the-counter supplement is advisable because most patients cannot possibly eat the amount of cruciferous plants necessary to achieve therapeutic dosages of indole-3-carbinol. I recommend 200 mg B.I.D. with food.
- b) Magnesium is an important cofactor for the catechol-O-methyltransferase enzyme that methylates 2-OH and 4-OH estrogens. These methylated compounds can subsequently be excreted from the body in the urine and in bile. The B vitamins and folic acid are also involved in these methylation reactions as well as other conjugation reactions in Phase II detoxification. Because many individuals possess genetic polymorphisms that interfere with their ability to metabolize folic acid to the active form used by the body, a metabolically active form of folate such as 5-methyl tetrahydrofolate should be administered. Magnesium can be taken at 200–400 mg per day. B vitamins should be 1000–5000% of the R.D.A., while folate can safely be taken at a dose of 1600 mcg for a 3–6 month trial of therapy. Folate should not be taken in dosages of more than 1 mg for an extended period of time.
- c) Oral enzyme therapy can assist in the destruction of uterine masses. The theory is that digestive enzymes such as lipase, pancreatase, trypsin, chymotrypsin, and other proteolytic enzymes produced by the pancreas, if taken on an empty stomach, will be absorbed into the bloodstream intact and assist in the enzymatic removal of superfluous tissue. Two capsules of an enzyme supplement should be taken with each meal as well as on an empty stomach between meals several times per day.

3. **Herbal Medicine:** There are 2 viable approaches to the use of herbal medicine with regard to leiomyomas that differ widely in theoretical premise. A Western approach bases herbal use primarily on the physiologic effect sought, while the Traditional Chinese Medicine (TCM) seeks to effect changes that are

described metaphorically. Both systems are viable and achieve results with few side effects.

- a) Phytoestrogens are plant compounds similar in shape to the estrogen molecule and can bind to estrogen receptors. They are much weaker than endogenous estrogens and have been shown, through competitive inhibition, to prevent the receptor binding of more potent estrogen and estrogen metabolites. (8,9) A pilot trial by the Functional Medicine Research Center reported December, 2002 on an estrogen balancing supplement that was able to demonstrate a significant decrease in symptoms of menopause by increasing the ratio of 2-OH to 16 α -OH ("good" to "bad" estrogen). The supplement contained phytoestrogens from red clover and kudzu, rosemary extract, curcumin, resveratrol (*Polygonum cuspidatum*) and other nutrient factors that included methylated folic acid.* Although it was menopause and not fibroids that was studied, the results nonetheless demonstrate the ability to modify estrogen balance with an herbal supplement combination. There are many herbs that have a hormone balancing effect that include black cohosh, chasteberry, dong quai, licorice and ginseng.
- b) In TCM, uterine fibroids are considered to be blood stasis in origin. In my practice I use a Kam-po** product containing Cinnamon and Hoelen (Keishi-bukuryo-gan; Gui Zhi Fu Ling Wan). This formula is standardized to contain 18.9–35.3 mg/day of Amygdalin, 67.3–125.2 mg/day of Paeoniflorin, and 1.02–2.39 mg/day of Cinnamic acid. Cinnamon (Gui zhi), the chief herb, unblocks the blood vessels and reduces blood stasis by promoting circulation. Peach Pit (Tao ren), Peony Root (Shao yao), and Moutan Bark (Mu dan pi) invigorate blood, break up and dispel blood stasis, and disperse accumulation. Mu dan pi helps to disperse heat that can transform out of stagnation. It is excess heat that can cause metrorrhagia and menorrhagia. Dampness may also contribute to the formation of masses and/or blood stasis, so Hoelen (Fu ling) is included to tonify the spleen to resolve dampness. A study in the *American Journal of Chinese Medicine* demonstrated a decrease in leiomyoma size in about 60% of patients after using this formula. (10)

*This supplement is "Estrobalance" and produced by Metagenics.

** Kam-po is the Japanese production of TCM formulations that are licensed by the Japanese Ministry of Health and Welfare, and manufactured under strict quality assurance. These formulations are standardized to contain consistent levels of bioactive markers of key herbs in each formula.

4. **Acupuncture:** Acupuncture is useful to balance the meridians and organs. Points needed depend upon the presenting clinical picture.

- a) For blood stagnation the following prescription can be employed: Zhongji (Ren 4), Guilai (S 29), Xuehai (Sp 10), Taichong (Liv 3). Ren 4 helps to regulate the Chong and Ren meridians and unblock the lower jiao. Stomach 29 is a local point to remove blood stasis from the uterus. Spleen 10 and liver 3 together regulate liver qi to relieve stasis and stagnation. I often find that liver 14 is also tender to palpation and will employ its use to aid in eliminating liver qi stagnation.
- b) For metrorrhagia due to excessive heat, Yinbai (Sp 1) and Ququan (Liv 8) can be added.
- c) For metrorrhagia due to spleen deficiency Zusanli (S 36) and Sanyinjiao (Sp 6) are appropriate additions to the basic point prescription.

5. **Vaginal Depletion Packs:** A vaginal depletion pack is a phytochemical application to the uterine cervix. This form of treatment has been used by naturopathic physicians for over 100 years. The treatment consists of applying a combination of magnesium sulfate, *Hydrastis Canadensis*, *Thuja*, *Melaleuca alternifolia*, vitamin A palmitate, bitter orange, and ferrous sulfate to a tampon that is placed directly against the cervix. After 24 hours the patient removes the pack. Vaginal depletion packs work by the action of the herbs which have a hygroscopic effect, aiding in the removal of fluid and lysed debris from the uterus. A normal course of therapy consists of one pack per week for 8 weeks, then every other week for 16 weeks.

The recommended treatment plan should be undertaken for a period of 16 weeks. This duration provides ample time for hormonal alterations to decrease leiomyoma size. The above protocol also requires weekly office visits for 8 weeks, followed by visits every other week for 8 more weeks. The office visits are for acupuncture and the placement of vaginal depletion packs. This ongoing contact also provides the opportunity to monitor patient compliance regarding dietary and supplement recommendations. Adopting a plant-based diet should be considered a permanent lifestyle modification because it is probable that fibroids will grow back if the patient returns to the behavior that likely created them in the first place.

Although periodic bimanual examination of the uterus can help identify a change in size of the uterus and any masses, a pelvic ultrasound should be performed at the completion of therapy to determine effect. A complete elimination of leiomyomas is not expected and would

be unusual. Treatment can be considered adequate if there is symptomatic relief and no increase in fibroid size, and quite successful if there is any size decrease at all. Recall that conventional treatment options are quite limited and carry significant risk.

Metrorrhagia can be severe and lead to disabling anemia, and if prolonged, even death. Intermenstrual bleeding must be significantly reduced or stopped quickly. If this is not accomplished, heroic intervention is necessary. It is not unusual for these women to require blood transfusions.

CONCLUSION

Uterine leiomyomas are one of the most common gynecologic complaints confronting health care providers. They can cause infertility, a great deal of suffering and almost one in three women undergoing hysterectomy have a diagnosis of uterine fibroids. A detailed understanding of contributing factors involved in fibroid formation allows for a comprehensive treatment approach. The all-inclusive therapy described in this article is necessary for long-term successful treatment of leiomyomas because their pathogenesis seems dependent upon fluctuations in hormone levels that are affected by everything from diet to environmental chemical exposure. By addressing all reasonable causative factors, a practitioner maximizes the likelihood of a favorable treatment outcome.

For Indole-3-Carbinol, methylated folic acid, magnesium and oral enzymes:

Metagenics
100 Avenida La Pata
San Clemente, CA 92673
800-692-9400

Thorne Research
PO Box 25
Dover, Idaho 83825
800-228-1966

For Vaginal Depletion Pack Salve:

Eclectic Institute
36350 SE Industrial Way
Sandy, Oregon 97055
800-332-4372

For Kampo Herbs:

Honso USA, Inc.
1438 W. Broadway Rd, Suite B-210
Tempe, AZ 85282
888-461-5808

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