Curcumin a New Modality for Treatment of Uterine Myoma

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Abstract: Curcumin is known for its antitumor, anticancer, strong anti-inflammatory, antioxidative, antiangiogenic, proapoptotic, antiamyloid, antiarthritic, potent inhibitors of cytochrome p450, reduced cholesterol level. Uterine fibroid are the most common pelvic tumors and occur in 20 to 25% of premenopausal women .Current pharmacological therapies include gonadotrophin releasing hormone GnRH agonists/antagonists, oral contraceptive, progestin selective modulator of progesterone receptor(Asppriśnil) and mifipristone.The aim of this work is to use for the first time in the literature curcumin for treatment of uterine myoma. A total of 50 women had uterine myoma were enrolled in the study, the inclusion criteria were age between 20-35 yrs mean age 32±3.25, no more than (3) intramural myomas the main diameter at 3 D transvaginal ultrasound >5mm. Curcumin is used in the tablet form each tablet 450 mg one tablet after meal 3 times daily for 12 weeks, assessment of uterine bleeding by using daily bleeding diapers and Hb concentration, uterine dimensions and myoma dimensions are measured by 3D ultrasound. Result we found statistically significant decrease in the uterine volume and myoma volume (cm3) $p<0.001$, again we find statistically significant increases in Hb percentage after treatment (p <0.05) the bleeding stop completely in 88% after 2 weeks treatment and after 4 weeks in 12% of the cases In conclusion, curcumin is a new drug with multiple pharmacological actions, no reported side effects of significances for treatment of myoma.
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Keyword: curcumin, mayoma, medical treatment

1. Introduction:

Curcumin (C_{21} H_2O O_6)[1] is known for its antitumor, anticancer [2-3] strong anti-inflammatory [4], antioxidative [4,5], antiangiogenic [5], proapoptotic [6], antiamyloid [7], antiarthritic [8], potent inhibitors of cytochrome p450, reduced cholesterol level.

Curcumin is the principal curcuminoid of the Indian curry [9] spice turmeric; curcumin can exist in at least two turmeric forms [10], keto and enol. The enol form is more energetically [11] stable in the solid phase and in solution. Curcumin is the main biologically active phytochemical compound of turmeric, it is extracted, concentrated, standardized and researched for it renowned range of disease prevention.

Uterine fibroid are the most common pelvic tumors and occur in 20 to 25% of premenopouaal women [12]

The clinical complications (menstrual disorder, anemia, pelvic discomfort, infertility and recurrent abortion) negatively affected women's health uterine fibroids are the most important indication for hysterectomy.

Pathologically uterine fibroids are benign tumors that arise from a single uterine smooth muscle cell, the growth of the tumor under the influence of local growth factors and sex hormones (estrogen and progesterone) [13] .The etiology is not clearly understood although several genetic and environmental factors have been proposed[14]

As no effective medical treatment is currently available [15] the main stay for treatment is surgery [16].

Current pharmacological therapies include gonadotrophin releasing hormone GnRH agonists/antagonists, oral contraceptive, progestin selective modulator of progesterone receptor(Asppriśnil) and mifipristone.

GnRH agonists inhibit steroidogenesis and induce mechanical menopause and can reduce fibroid volume up to 40 % in 3 months with a dramatic improvement in clinical symptoms [13] unfortunately, these effects are short lived since the use of GnRH agonists can only be temporary 3-6 months [17]

Decreased bone minerals is a common adverse events that can occur if GnRH agonist treatment is used for more than 6 months , Hot flashes, vaginal dryness, irregular bleeding, headache, depression , hair loss and musculoskeletal stiffness, manifestation of hypoestrogenemia, Gonadotrophin releasing hormone agonists are considered to be viable short term therapies, based on their adverse event profile and risks associated with long term decrease in estrogen and progesterone, moreover myoma regrowth occur after therapy is discontinued , so a need for a new therapy that avoid the previous complications is needed.

2. Material and Methods

50 women had uterine myoma were enrolled in the study, the inclusion criteria were age between 20-

35 yrs mean age 32±3.25, no more than (3) intramural myomas the main diameter at 3 **D** transvaginal ultrasound >5mm**.**

Curcumin is used in the tablet form each tablet 450 mg one tablet after meal, 3 times daily for 12 weeks, assessment of uterine bleeding by using daily bleeding diapers and Hb concentration, uterine dimensions and myoma dimensions are measured by 3D ultrasound.

The exclusion criteria were metabolic infectious diseases and Previous hormone therapy over the previous 9 months and history of previous operations and history of previous myomectomy history exclusion of combined adenomyosis and fibroids, aspirin intake and anticoagulant therapy and antihypertensives)

Ethics:

Informed Consent and explaining all the details of the procedure to the patients, and all procedures involving human subjects complied with the declaration of Helsinki 1975 and revised in 2000, again all the procedures accepted from the ethical committee of Heliopolis research center and Heliopolis Hospital.

Aim of the Work

The aim of this work is to use for the first time in the literature curcumin for treatment of uterine myoma The main objective was to assess the efficacy (reduce uterine volume, myoma volume, and uterine bleeding, and it's safety regarding the adverse effect and the cost of the treatment.

3. Results

Fifty women had uterine myoma were enrolled in the study, the inclusion criteria were age between 20-35 yrs, no more than (3) intramural myomas the main diameter at 3 **D** transvaginal ultrasound >5mm, Curcumin is used in the tablet form each tablet 450 mg one tablet after meal 3 times daily for 12 weeks, assessment of uterine bleeding by using daily bleeding diapers and Hb concentration uterine dimensions and myoma dimensions are measured by 3D ultrasound.

Table l: represent the result of treatment. we found statistically significant decrease in the uterine volume and myoma volume (cm3) $p<0.001$, again we find statistically significant increases in Hb percentage after treatment $p<0.05$ the bleeding stop completely in 88% after 2 week treatment and after 4 weeks in 12% of the cases.

Table (1): Effect of curcumin treatment in 50 myomatous patients

Characteristics	Before	After	*P*
Uterine volume	414.1+44.3	201±33.1	<0.001
Myoma volume	169.8±13.7	18.7±2.3	<0.001
Hb concentration	7.3±1.6	13.2+21	<0.001

4. Discussion:

This is the first report of the use of *in vivo* curcumin for treatment of myoma and the associated symptoms e.g uterine bleeding. The base of our work depend upon our previous work in which we studied the effect of curcumin on Leiomyoma *in vitro* studies using primary leiomyoma and myometrial cell culture demonstrated that curcumin suppresses proliferates an induce apopoptosis in all leiomyoma in a dose dependent manner without having any similar effects on myometrial cells(18), these antiproliferative (2,3,5,6) effect of curcumin was characterized by decrease in the number of viable cultured cells the proliferating cell nuclear antigen PCNA- positive rate, and PCNA whereas the proapoptotic effect were evident by an increase in the terminal deoxy nucleotidyl transfer biotin dutp nickend labelings TUNEL) - positive rate, cleaved poly adenosime 5-diphosphate-ribose) polymerase expression and a decrease in B cell Cl 1/lymphoma 2(BCL-2) protein expression, also it inhibit the expression of major growth factor(1,5,7) including epidermal growth factor, insulin like growth factor transforming. growth factor B3 and the receptors in cultured leiomyoma cells and antagonize growth factor induced increase in rate of leiomyoma cell proliferation Cultured myometrial cells however no affection on growth factor and their receptor expression nor rates of cell proliferation. it acts by reducing uterine blood flow(5). The decrease in uterine blood flow has been proposed as an early mechanism leading to the reduction of leiomyoma and uterine volume.

A significant difference in PCNA/total cell culture and BcL2/BAX was detected in myoma after treatment with curcumin(6). Its anticancer effects (2, 3) arise from its ability to induce apoptosis (6) in cancer cell without cytotoxic effect on healthy cells. curcumin can interfere with the activity of the transcription factor NF-kB. Curcumin(4) may suppress MDM2 an oncogene involved in the mechanisms of malignant tumor formation. [18]

It was found that the ultrastructural comparison of uterine myoma cells before and after treatment with curcumin decreased in mitochondrial swelling, myofilament content is decreased >75.5%, the mitochondrial swelled 4 times or more of their original size, no Lysosomal bodies within the cytoplasm after curcumin treatment and indicating

intracellular digestion of damages organelles. [18]

The Anti-inflammatory properties of curcumin is effective(4) in treatment of myoma and are potent inhibitors of cytochrome P450 and so reducing the level of estrogen(8). Curcumin may suppress MDM2, an oncogene involved in mechanisms of malignant tumor formation(2,3).

Curcumin might inhibit the accumulation of destructive beta-amyloid in the brains of diseases[7]. There is also circumstantial evidence that curcumin improves mental functions from colon cancer. cancer and carcinogenic effects may prove curcumin also activate p53[19].

No reported side effect expect in 2 cases complaining of some stomach pain and one of gall bladder pain which had a gall stone so, the drug should not be taken in cases of gall stones.

Conclusion

In conclusion, we are now on a verge of a new drug with multiple pharmacological actions, no reported side effects of significances for treatment of myoma, further randomized studies and large number population are needed to evaluate the efficacy and safety of this new treatment.

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