

Uterine Leiomyomas- Studies on Etiology, Ultrasound Diagnostics and Surgical Treatment

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ABSTRACT

Uterine leiomyomas constitute a substantial health issue for women and these benign tumors represent the most common single indication for hysterectomy. Leiomyomas have a major impact on economic costs and the quality of life of the patient.

Vitamin D is a potent anti-proliferative and immunomodulatory secosteroid hormone. Apart from its well-established role in the maintenance of calcium homeostasis, vitamin D modulates cell proliferation, differentiation, cancer invasion and angiogenesis. Despite extensive research on the role of vitamin D in the inhibition of cell growth in a large variety of tissues, there are no reports concerning the possible growth-modulatory effects of vitamin D on benign uterine tumor cells. The first aim of the present study was to assess the potential effect of 1,25(OH)₂D₃ and 25(OH)D₃ vitamin D derivatives on the growth of leiomyoma and myometrial cells *in vitro*. Samples of leiomyomas and normal myometrial tissues were obtained from six premenopausal women with uterine leiomyomas undergoing hysterectomy. Paired cultures were established and the effect of these two compounds examined using a colorimetric crystal violet assay. Vitamin 1,25(OH)₂D₃ effectively and concentration-dependently inhibited the growth of myometrial and leiomyoma cells. Hypovitaminosis D may play a role in the etiology and growth of leiomyoma cells.

Manual palpation and estimation of the size of the uterus is an important part of the routine gynecological examination, as it is necessary to exclude abnormal growth of this reproductive organ due to benign or malignant tumors. The size of the uterus is also a crucial factor in assessing the method of hysterectomy most appropriate for the patient. The dominant practice is to estimate the size of the nonpregnant uterus by bimanual examination and compare it to a pregnant uterus of comparable size. However, only a rough estimate may be obtained by this method, and other more accurate means for the purpose have been developed. Gynecological ultrasound and use of the geometric formula of the prolate ellipsoid has been the most common means of estimating the uterine dimensions by imaging techniques. This method has also involved a potential for errors in estimation of uterine size.

The second aim here was to evaluate the accuracy of a new formula combining the prolate ellipsoid (uterine corpus) and cylinder (uterine cervix) formulas in estimating the preoperative weight of the total myomatous uterus, using a transvaginal ultrasound probe to obtain the uterine dimensions for the formulas. The third aim was to establish different sources of variation in these measurements using repeatability and reproducibility method. The length, width and anteroposterior diameter of the uterine corpus, and the length and anteroposterior diameter of the cervix were preoperatively determined using a transvaginal ultrasound probe in 12 women with symptomatic leiomyomas scheduled to undergo hysterectomy. Three investigators repeated all rounds of measurement three times, producing in total of 108 findings. The geometric formula of prolate ellipsoid was compared to a formula combining the ellipsoid and cylinder formulas for accuracy in predicting overall uterine size (corpus and cervix) through correlation with hysterectomy specimens.

The new combination formula was more accurate in predicting the true total weight of the uterus than the plain prolate ellipsoid formula, and the transvaginal ultrasound probe proved useful in evaluating the dimensions of the uterine corpus and cervix. Variation due to differences across trials

(repeatability), across physicians (reproducibility), and across patients (variability) was then estimated. The more experienced the physician was in taking the ultrasound measurements, the less deviation was observed between her own three measurements. The experience of the physician thus had an effect on repeatability (differences across measurements), but not on reproducibility (differences across physicians), in estimating uterine weight by ultrasound.

Surgery is the cornerstone of treatment for leiomyomas. Hysterectomy serves as a terminal procedure, while myomectomy is a treatment of choice for women who desire future pregnancies or otherwise wish to retain their uterus. The fourth aim was to evaluate the clinical effectiveness and safety of the enucleation of uterine leiomyomas by traction method via colpotomy. Ten women with menorrhagia, pelvic pain or secondary infertility associated with single uterine myomas underwent transvaginal myomectomy with screw traction by colpotomy. Traction myomectomy was completed vaginally in all patients. All women reported relief of their symptoms after a mean follow-up of 24 months. Three patients had a term delivery postoperatively. Traction myomectomy by colpotomy proved to be a feasible approach for selected patients wishing to preserve their ability to conceive. A single well-lined myoma of 5-8 cm diameter and accessible via colpotomy is a suitable subject for the procedure.

The fifth aim was to study long-term outcomes and hysterectomy rates after hysteroscopic endometrial resection with or without myomectomy for menorrhagia. Endometrial resection and concomitant hysteroscopic myomectomy was performed in 53 women involving submucous myomas with an intramural extension of less than 50 % and smaller than 5 cm in diameter. Each subject was matched with a patient who had no submucous myomas and who had been treated by endometrial resection only. During the mean follow-up period of 6.5 years, hysterectomy was performed in 26.9 % of the patients with myomectomy and in 17.0 % of those without ($p=0.22$). Most (75.6 %) of the 82 women who had not required hysterectomy had reached menopause. All the patients without hysterectomy in both groups reported amenorrhoea or slight bleeding, and this response persisted for years after the treatment. Endometrial resection may be combined with hysteroscopic myomectomy without a significant increase or decrease in hysterectomy rates during a long-term follow-up.

Iloista ja rentouttavaa joulunaikaa!

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