TITLE.

INHIBITION OF ANGIOGENESIS AND GROWTH FACTOR PRODUCTION IN COMBINATION WITH INDUCTION OF METALLOPROTEINASE ACTIVITY IN THE REGRESSION OF UTERINE LEIOMYOMAS AFTER A COURSE OF TREATMENT WITH ESMYA

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ABSTRACT.

Context. Clinical materials showed that treatment with UA (Esmya) results in increased apoptosis, inhibition of proliferative and mitotic activity of uterine leiomyomas (UL) cells. However, the significant UA-induced decrease in the size of UL which mainly consists of stroma allows suggesting that UA also affects angiogenesis and metabolism of extracellular matrix. Objective. The molecular and biological mechanisms of UA effects on UL have been mainly studied in vitro. Methods. The purpose of the study was to determine the molecular and biological mechanisms of UA effects on angiogenesis, production of growth factors and matrix metalloproteinases and their tissue inhibitors in UL in vivo. Patients & interventions. A histological and immunohistochemical study was performed in UL removed in 31 women after 3 months of treatment with selective progesterone receptor modulator ulipristal acetate, and in 10 female patients of similar age who did not receive hormonal therapy. Main outcome measures. UA was shown to reduce leiomyoma size not only due to induction of tumor cell apoptosis, reduction in their proliferative and mitotic activity but also due to inhibition of angiogenesis, production of growth factors (VEGF, EGF, FGF-2, TGF-ß1) in combination with increased production of matrix metalloproteinases (MMP-2, -10, -12) and decreased production of their tissue inhibitors (TIMP-1, -2, -3). Results. This results in the reduction of the vascular bed, remodeling and decrease in the volume of extracellular matrix of leiomyoma. Conclusions. The mechanisms of the fast, significant, and prolonged reduction in leiomyoma size are explained by the simultaneous negative effect that UA produces on the parenchymatous component, angiogenesis and extracellular matrix.

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