



Session PO1-2b - Gynecology II

T-047 - Effects of Vitamin D in Human Uterine Leiomyoma Growth in a Xenograft Animal Model.

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Categories

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Keywords

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Abstract

Introduction: Uterine leiomyomas (LM) are the most common benign estrogen-dependent tumor in women of reproductive age. Clinical observations have noted a correlation between the presence of LM and Vitamin D (VitD) deficiency. We have recently described that VitD exerts *in vitro* an antiproliferative action on human LM primary cells by cell growth arrest and Wnt/ β -catenin inhibition, suggesting VitD as an effective treatment to stabilize LM size. One step forward, here we claim to corroborate *in vivo* the effect of VitD in a xenograft mouse model for human LM based on described pathways and extracellular matrix (ECM) production.

Methods: Human intramural LM fragments (4x4mm) from the same patient were implanted intraperitoneal in ovariectomized NOD-SCID mice (with hormonal supplementation). After that, we established 3 groups: control (n=8), VitD 0.5 μ g/kg/day (n=8) and VitD 1 μ g/kg/day (n=8) (VitD micro-osmotic pumps for 21 days). Human LM implants were monitored and measured weekly by PET/CT using ¹⁸F-FDG. Finally, LM implants were collected, measured and analyzed by Western Blot (PRO-CASPASE3, COLLAGEN I and FIBRONECTIN) and by TUNEL assay.

Results: PET outcomes showed a dynamic reduction of ¹⁸F-FDG uptake (kBq/cm³) in VitD 1 μ g/kg/day group, being statistically significant at day 21 (p=0.0026). Post-treatment, human LM size implants did not decrease in control group while VitD significantly shrank LM size in 0.5 μ g/kg/day group (p=0.0398) as well as 1 μ g/kg/day group (p=0.0113). Functional analysis demonstrated a significant decrease of PRO-CASPASE 3 protein (p=0.0014) as well as an increase in apoptotic cells (Fold Change=3). Interestingly, VitD inhibited ECM proteins production (COLLAGEN I and FIBRONECTIN) in a dose-dependent manner.

Conclusion: VitD reduced metabolic activity of human uterine LM implants in the mouse model, suggesting a decrease in the proliferation rate. Along with this, the apoptosis induction as well as the inhibition of ECM protein production observed could explain the macroscopic LM size reduction noted. These findings would demonstrate the potential of VitD as an effective therapy to treat and reduce human uterine LM. AC & HF contributed equally. Support: PI15/00312; PI17/01039; CD15/00057; ACIF/2016/444