

New pathogenetic perspectives in Pelvic Organ Prolapse (POP): the possible role of the cross-talk between AGEs, MAPK and Smads

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Collagen and MMPs play a pivotal role in the pathophysiology of the Pelvic Organ Prolapse (1). In POP samples a switch between type I and type III collagen together with a simultaneous activation of MMPs have been observed and the main consequence of these changes is the loss of mechanical support in the vaginal wall (2). Aim of this study was to prove that AGEs induces the activation of MMPs through ERK1/2 and synchronically stimulates changes in collagen composition directly through Smads. The case group consisted of 20 patients suffering from stage III genital prolapse undergoing colpohysterectomy and anterior and posterior plastic vaginal surgery and 10 control patients treated with laparohysterectomy for uterine fibromatosis. Histological and Immunohistochemical analysis using AGE, RAGE, ERK 1/2, Smads 2-3, Smad 7, MMP-3 and collagen I-III were performed. AGE and ERK 1/2 were also evaluated using Western-Blot analysis. POP samples from anterior vaginal wall showed disorganization and a distortion of the normal muscularis architecture. In POP samples AGE, ERK 1/2, Smad 2-3, MMP-3 and collagen III were upregulated in muscularis whereas in controls Smad 7 and collagen I were increased in the same layer. RAGE was mild or absent both in controls and prolapse. In summary we suggest the possible role of these new markers in the pathogenesis of POP but further studies are required to elucidate if the change of these molecules is the reason or the result of POP disease.

References

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Keywords

Pelvic organ prolapse, AGEs, RAGE, MAPK, Smads