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MORPHOLOGIC AND METABOLIC ASSESSMENT OF ANTERIOR VAGINAL WALL AT DIFFERENT STAGES OF PELVIC ORGAN PROLAPSE

Hypothesis / aims of study

Collagen is the main component of endopelvic fascia and it is involved in the physiopathology of female organ prolapse (POP). Pelvic floor as any other supporting structure is actively remodeled as response to mechanical stress. Metalloproteinases (MMP) play a pivotal role into this process being responsible of collagen turnover. MMP expression and activation may vary according to endogenous and local stymuli. The research focused on MMP-2 and MMP-9 subtypes that seem to be involved in many diseases related to connective tissue laxity (1, 2, 3). Aim of this study is to correlate clinical staging of anterior vaginal wall prolapse to histological and metabolic assessment.

Study design, materials and methods

Anterior vaginal wall full thickness excisional biopsies including endopelvic fascia have been obtained during surgical procedures performed from January 2008 to January 2010. All the patients were in postmenopausal status and recurrences or vault prolapses have been ruled out. Specimens have been freshly cut for fixation and snap frozen in liquid nitrogen. Presence of POP was assessed according to the POP-Quantification. Samples have been subsequently divided into three groups: group A (controls), group B (prolapse stage I and II) and group C (prolapse stage III and IV). Formalin fixed samples have been embedded, cut and stained with Trichromatic Masson Goldner (TMG) stains. Light microscopy on TMG was performed to assess collagen amount, organization and composition. All parameters were scored semi-quantitatively by two blind observers on two areas of interest rapresented by vaginal mucosa and underlying fascia. MMP2 and MMP9 activity have been evaluated by gelatine zymography distinguishing active form from the pro-enzyme (inactive form). Statistical evaluation was made by One-Way ANOVA analysis of variance.

Results

Eightyfive patients have been biopsied. A complete evaluation panel (histology and zimography) was completed for sixtynine patients. Seventy biopises for histological assessment (7 group A, 25 group B, 38 group C), sixtynine biopsies for MMP-2 assessment (7 group A, 28 group B, 34 group C) and seventynine biopsies for MMP-9 assessment (9 group A, 30 group B, 40 group C) have been successfully processed. MMP-2 activity progressively reduced in groups A, B and C with a significant difference ($p<0.05$) between groups A and C. MMP-2 total expression increased in groups A, B and C respectively but without significant difference. Discrimination of active and inactive form of MMP-9 was not possible. Total expression of MMP-9 showed a decreasing but not significant pattern in groups A, B and C. Collagen amount progressively increased both in fascia and mucosa in groups A, B and C with a significant difference observed between group C and groups A and B in vaginal fascia ($p<0.05$) and between group B and group C in vaginal mucosa ($p<0.01$). Collagen fibres organization progressively increased both in fascia and mucosa in groups A, B and C with a significant difference between group C and group B in vaginal mucosa ($p<0.01$) and between group C and groups A and B in fascia ($p<0.05$).

Interpretation of results

Patients were arbitrarily divided in three groups: A (controls), B (early stages), C (advanced stages). According to our results there is some evidence that in patients with advanced stages of POP there is an increase of total collagen amount associated to a decrease of MMP-2 activity. Such observation correlates with the common finding of a subjectively thickened vaginal wall of patients affected by a III – IV stage prolapse (Group C). High stage prolapse is known to be a risk factor for POP recurrence and this observation could correlate with an altered metabolic setting of collagen, represented –in this series- by a lower MMP-2 activation ratio. In this study it was not possible to distinguish active form from total form of MMP-9 and no significant difference in expression of MMP-9 was reported. It could be explained by the observation that there is an intrinsic limitation of the technique and that the expression of MMP-9 in vaginal wall is low. Collagen amount and organization trends were more evident in epithelium than in fascia. This finding probably reflects the keratinisation that occurs when vaginal mucosa is exposed to the external environment. The study outlined a peculiar metalloproteinases behaviour at different prolapse stages. Further researches are necessaries to investigate the correlation between clinical outcome and metabolic changes in patients affected by pelvic organ prolapse.

Concluding message

These results supports the theory that there are some changes in morphologic pattern and collagenic metabolism of vaginal wall of women affected by POP and that the degree of changes varies according to the clinical staging.

References

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