254

Sottner O[1], Halaska M[1], Gabriel B[2], Benkova K[3], Maxova K[1], Hurt K[1], Vojtech J[1], Vlacil J[1], Zahumensky J[1], Kolarik D[1], Gitsch G[2], Kittnar O[4]

1. *Department of OB/Gyn, University Hospital Na Bulovce, First Faculty of Medicine, Charles University in Prague, Czech Republic,* ***2.*** *Department of OB/Gyn, Freiburg University Medical Centre, University of Freiburg, Freiburg, Germany,* ***3.*** *Department of Pathology, University Hospital Na Bulovce, Prague, Czech Republic,* ***4.*** *Institute of Physiology, First Faculty of Medicine, Charles University in Prague, Czech Republic*

CHANGES IN COLLAGEN IV EXPRESSION PATTERN IN UTEROSACRAL LIGAMENTS OF PATIENTS SUFFERING FROM PELVIC ORGAN PROLAPSE AND STRESS URINARY INCONTINENCE.

Hypothesis / aims of study

The aim of this study is to describe and compare the expression of extracellular matrix proteins in the uterosacral ligaments of women with and without pelvic organ prolapse in order to clarify its pathogenesis.

Recent studies indicate that pelvic organ prolapse can, at least in part, be defined as a connective tissue disease. High rates of pelvic organ prolapse and urinary incontinence were found in patients suffering from connective tissue disorders (e.g. Marfan syndrome and Ehlers-Danlos syndrome) and there is some evidence that abnormalities of the connective tissue composition may contribute to the genesis of pelvic organ prolapse in all patients. The uterosacral ligaments are an important part of the pelvic support system and establish the level 1 support of the cervix and the upper vagina. As such the extracellular matrix composition of the uterosacral ligaments could play an important role in pathogenesis of the uterine prolapse.

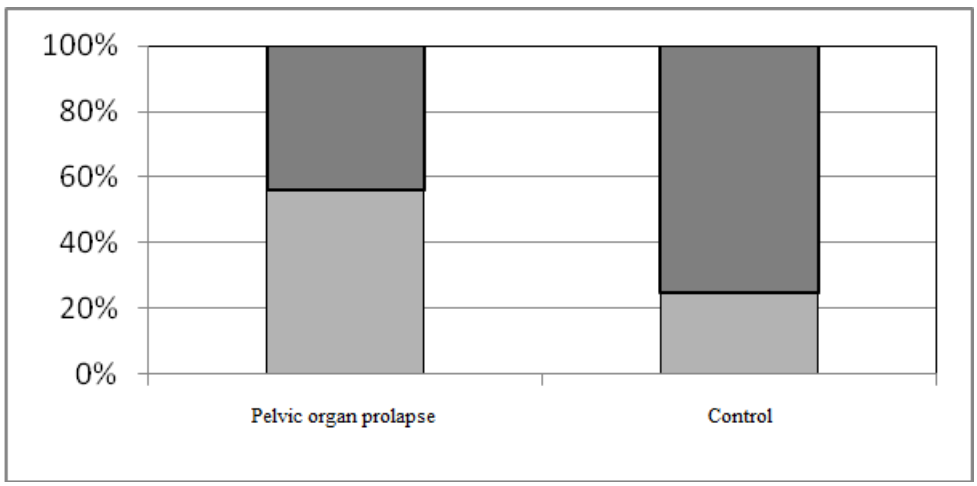
Study design, materials and methods

We investigated the set of 162 women who underwent hysterectomy. Our set consisted of 80 women operated for pelvic organ prolapse and 82 control females with no significant pelvic organ descent (ICS POP-Q stage 0, 1) but suffering from any other benign disease of a genital tract (e.g. menorrhagia). The significant pelvic organ prolapse was defined as ICS POP-Q stage 2 or more. Pelvic malignancies were excluded. Biopsies of the right and left uterosacral ligaments were obtained during hysterectomy. The biopsies were performed at the level of the cervical insertion of the uterosacral ligament using a standardized technique. All biopsy specimens were fixed in formalin and embedded in paraffin. The standardized immunohistochemical protocols were used. A panel of extracellular matrix proteins was evaluated by immunohistochemistry. Monoclonal antibodies against collagen I, II, III, IV, V, VI and against MMP-1, MMP-2, MMP-9, MMP-13 (Medicorp Inc., Canada); monoclonal antibody against laminin (Dako, Denmark) and polyclonal antibody against fibronectin (Dako, Denmark) were used. All slides were separately examined by two experienced pathologists blinded to the clinical diagnosis. Minimal or no staining reaction was scored as (-), a weak reaction was scored as (+) and a strongly positive staining reaction was scored as (++). The data were analyzed and the groups were compared. For statistical analysis, ANOVA - Analysis of variance and Fischer´s exact test were used.

Results

The left and right uterosacral ligaments of 162 women were analyzed. There was a significant change in collagen IV expression. Statistically significant higher expression of collagen IV was found in patients suffering from pelvic organ prolapse compared to controls – $p<0.001$ (Graph 1). The same finding was also noticeable when comparing the group with significant descent in the anterior compartment to controls – $p<0.0001$, the group with significant descent in the posterior compartment to controls – $p<0.0001$ and the group with significant descent in the central compartment to controls – $p<0.0001$. Moreover, the same trend was demonstrated in comparison of the group with significant stress urinary incontinence to controls – $p=0.0015$. By contrast, no such difference was found neither in relation to the demographic parameters (age – $p=0.15$; body mass index – $p=0.67$), nor to the parameters of personal history (duration of menopause – $p=0.62$; gestation - $p=0.11$; parity - $p=0.58$; history of any hernia – $p=0.78$; hormone replacement therapy use – $p=1$ or smoking – $p=1$).

Similar findings were not proven for any of the other extracellular matrix proteins of the uterosacral ligaments.



Graph 1: Significantly higher expression of collagen IV was found in the uterosacral ligaments of women suffering from pelvic organ prolapse.

Interpretation of results

The expression of the collagen IV in the extracellular matrix of the uterosacral ligaments seems to be significantly different (higher) in patients suffering from the pelvic organ prolapse and/or the stress urinary incontinence. There is no such difference in dependence on age, body mass index, duration of menopause, gestation, parity, history of any hernia, hormone replacement therapy use or smoking. This finding supports the hypothesis of tissue composition significance in pathogenesis of the pelvic organ prolapse and stress urinary incontinence, although it does not elucidate what is the cause and what is the consequence.

Concluding message

We demonstrated the significantly higher expression of collagen IV in the extracellular matrix of the uterosacral ligaments in females suffering from pelvic organ prolapse and/or the stress urinary incontinence.

Specify source of funding or grant	**Our project was financed by the Grant IGA of The Ministry of Health of the Czech Republic No. 9299-3/2007.**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Local Ethics Committee of the University Hospital Na Bulovce, Czech Republic**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**