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Radziszewski P. [1], Borkowski A. [1], Torz C. [1], Bossowska A. [2], Gonkowski S. [2], Majewski M. [2]
1. Department of Urology, Medical Academy of Warsaw, 2. Department of Clinical Physiology, UWM Olsztyn, Poland

COLLAGEN V AND VII DISTRIBUTION IN URETHRAL SUPPORTIVE MECHANISM OF THE STRESS INCONTINENT WOMEN WITH AND WITHOUT ESTROGEN THERAPY

Aims of Study

It was demonstrated by Keane et al. that the periurethral connective tissue of nulliparous women with stress incontinence contained significantly less collagen, in comparison with the continent control. They have also demonstrated a decrease in the collagen type I to type III ratio. A significant reduction of type I collagen has also been demonstrated in the pubocervical fascia of incontinent women. Falconer et al. found changes in the collagen metabolism in pre-menopausal, stress-incontinent women, primarily expressed by higher levels of mRNA encoding collagen type I and/or III, which, in turn, may be responsible for generating more rigid extracellular matrix, resulting in the impairment of connective tissue mechanical functions .

In contrast, no major changes in collagen metabolism have been found in stress incontinent women after the menopause, however their paraurethral connective tissue was found to be estrogen-sensitive .

The proper distribution and structure of the collagen fibers within the arcus tendineus fasciae pelvis (ATFP) may play a crucial role in the protection of the normal intraabdominal/intrapelvic positioning and orientation of the female urinary bladder-urethra complex and for the proper pressure transmission within the bladder neck and urethra. While all above-mentioned studies have focused on the occurrence and distribution of collagen type I and III, which are considered to be the most common types found in the connective tissue, no study described collagens V and VII distribution. These two types of collagen are thought to be responsible for the proper three-dimensional orientation of structural type I and III collagens.

Methods

Fifty post-menopausal female patients (mean age of 61.7$\pm$7.2) with a history of urinary incontinence were included in the study, after signing the informed consent. The Local Institutional Review Board approved the experimental protocol.

Urinary incontinence was diagnosed during the standard urodynamic procedure, accordingly to the ICS guidelines. Patients with genuine stress incontinence were offered surgical treatment (open Burch colposuspension) after the examination, either immediately or after a 3-month-long estrogen therapy with estriol (0.5mg, intravaginally, twice a week). Patients suffering of either mixed (i.e., stress and urge) or urge incontinence were excluded from the study. Age-matched patients without any form of incontinence (as verified by patient's history and one-hour pad-test) undergoing surgery within the small pelvis served as control group (mean age 65.8$\pm$5.1, n=8).

The specimens of ATFP and vagina musculi recti abdominis (VMRA) were collected during the Burch procedure or during other surgical procedures (control group) by means of cold-cut biopsies. Specimens of interest were collected from three groups of patients: age-matched controls (CONTR), patients with SUI without local estrogen therapy (NON-ESTR) and patients with SUI after 3 months course of intravaginal estrogen therapy (ESTR). Tissue samples were then processed for either single or double immunofluoresecence by means of anti-collagen V (C_5) and/or anti-collagen VII (C_7) antibodies (both from Sigma, Germany, dilution: 1:500 and 1:300 respectively).

Results

Genuine stress urinary incontinence (SUI) were found in 23 of 50 examined women, 12 patients had mixed stress and urge incontinence and 7 women suffered from pure urge incontinence. In thirteen patients no urinary incontinence could be objectively demonstrated. Out of 23 women with SUI, 3 did not decided to have the surgical treatment of the incontinence (they were offered physiotherapy). The remaining 20 women were randomly selected for the group receiving intravaginal estrogen treatment and subsequent open Burch colposuspension (ESTR) or Burch colposuspension alone (NON-ESTR). After 3 months none of patients from the ESTR group regained full continence without subsequent Burch colposuspension.

Immunochemical demonstration of collagen V in studied tissues.

No obvious differences were found in the distribution pattern of C_5-IR structures in sections of VMRA specimens obtained from CONTR, ESTR or NONESTR group . In each group immunopositive fibers emitted bright red fluorescence, clearly different from the weak background signal. These fibers ran parallel to each other, being organized in distinct bundles, giving a typical picture of a fibrous connective tissue. However, the organization of C_5-IR fibers in the Cooper's ligament was severely affected by degenerative processes

accompanying the urine incontinence, resembling in detail situation observed when anti-C_7-serum was used. While in the specimens obtained from healthy volunteers the distribution and organization of these fibers resembled that observed in the VMRA in patients from NONESTR group the degeneration of these connective elements ranged from relatively light degree to severely disturbed status, where the structure of only single C_5-IR (and simultaneously C_7-IR) fibers appeared not to be affected by degeneration. Within the ESTR group the degree of C_5-IR connective fibers disintegration were differently expressed, ranged from that observed in the NONESTR group to relatively good preserved structure. However, Cooper's ligaments sections from the ESTR group always showed disturbances in the distribution, structure and preservation of the meshwork of C_5/C_7-IR fibers when compared to the fibrous connective elements observed in the control group.

Immunochemical demonstration of collagen VII in studied tissues.

The distribution pattern of C_7-IR material in the human VMRA resembled this observed for C_5 in each of group studied, giving the picture of an almost total co-localization. Only sporadically, some collagen fibers appeared to be constituted exclusively by C_7-IR material .

Conclusions

Connective tissue of women with SUI demonstrated a degenerative pattern of collagen V and VII-containing filaments distribution, which may be responsible for an altered biomechanical properties of this tissue.

These changes were restricted to the urogenital suspensory apparatus alone and were not observed within the somatic fasciae.

Furthermore, it appears that long-term estrogen therapy could play, at least partly, a protective role for the connective tissue within the small pelvis.

References:

Keane D.P., Sims T.J., Abrams P. et al. Br. J. Obstet. And Gynecol. 104: 994-998, 1997.

Falconer C., Ekman-Ordeberg G., Blomgren B. et al. Acta Obstet. Gynecol. Scand. 77:95-100, 1998.