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INCREASED ELASTIN CONTENT IN THE VAGINAL WALL OF POSTMENOPAUSAL WOMEN WITH PELVIC ORGAN PROLAPSE

Hypothesis / aims of study

Changes in elastin content have been linked to the pathophysiology of pelvic organ prolapse (POP), however it is unclear whether the elastin content is increased [1] or decreased [2,3]. Such discrepancies could be attributed to differences in biopsy site, kind of analysis and/or patient population. Our study is the first to perform an extended biochemical analysis of different elastin features in tissues from the anterior vaginal wall of postmenopausal Caucasian women with and without POP. We aimed to compare elastin content, cross-linking, post-translational modification, and enzymatic degradation profiles of the (normal) precervical region and the prolapsed anterior vaginal wall tissues of women with POP. These data were compared to tissues from the precervical anterior vaginal wall of controls without prolapse to identify features specific to POP in the different parameters evaluated.

Study design, materials and methods

After informed consent, full-thickness anterior vaginal wall biopsies were collected from Caucasian postmenopausal women without hormonal therapy. Cases were 5 POP patients undergoing POP surgery (anterior repair for cystocele POP-Quantification stage ≥ 2). Each case was her own control as vaginal wall biopsies during anterior colporraphy were taken from the POP site (POP group/POP site, n=5) and non-POP site (POP group/non-POP site, n=5). Controls were 5 parous women without POP undergoing hysterectomy, where biopsies were taken from the anterior part of the vaginal apex after hysterectomy (no POP group/ controls, n=5). Elastin was isolated and the amount per mg of dry tissue was calculated. LC-MS analysis was used to quantify tetrafunctional cross-links (desmosine/isodesmosine). Pancreatic elastase digested material was used to semi-quantify the hydroxyproline content of three hydroxylated peptides (P283; P347;P580) and their non-hydroxylated counterparts by mass spectrometry; and to compare the enzymatic degradation profiles. Mann-Whitney or Wilcoxon matched-pair signed rank tests were used for statistical analysis. The peptide digests were analyzed using Progenesis QI software, followed by an ANOVA test of the transformed normalized abundances of the peptides. The tissues collected for this study were redundant after surgery and not subject to Ethical Committee approval.

Results

Tissues from the POP group/POP site contained twice the amount of elastin compared to samples from the no POP group (**, p=0.0079), and the POP group/non-POP site (marginal; p=0.0625). The desmosine/isodesmosine quantification revealed no significant differences between the different groups. The hydroxylation degree of the three proline residues that were chosen for analysis was similar in all groups (Table 1). From the peptides that were identified in the enzymatic digest, only 6.8% (93 out of 1375) differed significantly in their normalized abundances between the three groups.

Interpretation of results

We found higher elastin content in vaginal wall biopsies of postmenopausal women with POP, which seems to be specific to the prolapsed tissues. This finding corroborates previous reports that postmenopausal women with POP, and without hormonal therapy, have increased elastin content in the prolapsed tissues [1]. Our original study design allowed us to make comparisons with two different controls: tissues from women with the same hormonal status and *without* POP, and non-prolapsed tissues from the same women *with* POP. Our data suggests that the alteration of the elastin content is specific to prolapsed tissues and does not seem to be related to alterations in the tetrafunctional cross-links or to the post-translational modification of proline hydroxylation of elastin. Interestingly, the differences in the enzymatic cleavage between POP patients and healthy individuals suggest small differences in susceptibility towards enzymatic cleavage. Such differences could be due to structural variations in the samples as a result of damage in the elastin fibers in prolapsed tissues. This is an indication that elastin from patients with POP might be pre-damaged and as a consequence be cleaved more easily into smaller peptides. The combination of our results supports the theory of altered elastin metabolism in women with POP.

Concluding message

Our findings support the theory that postmenopausal women with POP show changes in elastin. We provided evidence of increased elastin content in the prolapsed tissues and showed small differences in susceptibility towards enzymatic cleavage.

Table 1. Biochemical features of elastin

Feature	A **No POP/ controls (n = 5)**	B **POP group/ non-POP site (n = 5)**	C **POP group/ POP site (n = 5)**	A-B‡ **p-value**	A-C‡ **p-value**	B-C† **p-value**
Elastin[a]	2.9 (2.3 – 5.7)	3.1 (2.4 – 5.9)	6.1 (5.2 – 7.9)	1.0000	0.0625	0.0079
DES/IDES[b]	17.9 (11.3 – 23.8)	17.6 (13.2 – 19.2)	20.8 (18.8 – 22.5)	1.0000	0.3095	0.1250
Hydroxylation degree[c]						
P283	41.1 (36.9 – 44.8)	41.8 (37.2 – 44.9)	42.8 (37.8 – 47.6)	1.0000	0.5476	0.6250
P347	22.3 (21.2 – 23.6)	23.3 (20.7 – 28.3)	22.5 (18.8 – 34.2)	0.5476	0.8413	0.8125
P580	52.9 (49.6 – 56.6)	53.8 (50.5 – 58.4)	54.9 (48.9 – 64.3)	0.8413	0.5476	0.6250

DES: desmosine; IDES: isodesmosine. Data are presented as the median (IQR) and are the % of dry weight[a], µg/mg of elastin[b], or the % of hydroxylation degree[c] of three proline residues. Non-parametric statistical tests: Mann-Whitney‡ or Wilcoxon matched-pair signed rank test†.

References

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Disclosures

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