Int Urogynecol J (2004) 15: 266–271
DOI 10.1007/s00192-004-1150-z

ORIGINAL ARTICLE

**Leonardo R. P. S. Bezerra · Paulo C. Feldner Jr
Lea M. Kati · Manoel J. B. C. Girão
Marair G. Sartori · Edmund C. Baracat
Geraldo Rodrigues de Lima · Helena B. Nader
Carl P. Dietrich**

Sulfated glycosaminoglycans of the vagina and perineal skin in pre- and postmenopausal women, according to genital prolapse stage

Received: 3 September 2003 / Accepted: 20 February 2004 / Published online: 19 May 2004
© International Urogynecological Association 2004

Abstract The aim of this study was to analyze the amount and types of sulfated glycosaminoglycans (GAGs) of the extracellular matrix (ECM) in the posterior vaginal wall and perineal skin in menacme and postmenopausal women, according to genital prolapse stage. Samples of vaginal tissue and perineal skin were obtained from 40 women who underwent vaginal surgery. Sulfated glycosaminoglycans were extracted by extensive tissue maxatase digestion, submitted to electrophoresis on agarose gel, and their concentrations were determined by densitometry. Dermatan sulphate (DS) was the predominant GAG, followed by chondroitin sulfate (CS) and heparan sulfate (HS). In the vagina there was a significant decrease in total GAGs, CS, DS and HS in postmenopausal women with prolapse stage 2 and 3 compared to the premenopausal group, independent of the stage. In stage 2 and 3 postmenopausal patients there was a significant decrease of DS and HS compared to the stage 1 postmenopausal group. In perineal skin there was no significant difference between total GAG amount, DS and HS. However, the amount of CS in premenopausal stage 1 patients was significantly than that in postmenopausal patients stage 1 and stages 2 and 3. In conclusions, there are quantitative and qualitative differences in GAGs of the ECM in vaginal wall and perineal skin between women in menacme and the postmenopause, according to genital prolapse stage.

L. R. P. S. Bezerra (✉) · P. C. Feldner Jr · L. M. Kati · M. J. B. C. Girão · M. G. Sartori · E. C. Baracat · G. R. de Lima
Section of Urogynecology and Pelvic Surgery,
Department of Gynecology, Federal University of São Paulo,
Rua dos Otonis 567, Vila Clementino, São Paulo, Brazil
E-mail: leosobreira@uol.com.br
Tel.: +55-11-50842514
Fax: +55-11-50842514

H. B. Nader · C. P. Dietrich
Department of Biochemistry, Federal University of São Paulo,
São Paulo, Brazil

Keywords Extracellular matrix · Genital prolapse · Glycosaminoglycans · Postmenopause

Abbreviations CS: Chondroitin sulfate · DS: Dermatan sulphate · ECM: Extracellular matrix · GAG: Glycosaminoglycan · HS: Heparan sulfate · PBS: Phosphate-buffered saline

Introduction

Genital prolapse is a common condition and a major cause of gynecological surgery. The pathogenesis is not fully understood. In women with genital prolapse abnormal connective tissue metabolism has been shown. Several lines of research indicate changes in both the structure and the biochemical composition of the connective tissue, especially in the collagen component [1, 2, 3]. The findings are, nevertheless, contradictory.

Although collagen fibers are the main component of the extracellular matrix (ECM), other macromolecules, including elastic fibrils, and a gel of proteoglycans and glycosaminoglycans, account for the functional properties of connective tissue [4]. Proteoglycans are monomers that course between the collagen fibrils and consist of a core protein linked to one or more polysaccharides called sulfated glycosaminoglycans (GAGs). These are linear carbohydrate polymers which consist of repeating disaccharide units (hexosaminyl-uronyl or hexosaminyl-galactosyl sugar residues) in which one (or both) contains a sulfate residue [5]. Some of the most common GAGs are heparan sulfate (HS), chondroitin sulfate (CS) and dermatan sulfate (DS). GAGs are important components of the cell surface and ECM, and interact specifically with other matrix components and growth factors. These interactions are responsible for the structural organization of the ECM and the regulation of cell–cell and cell–matrix interaction [6]. The relationship between GAGs, menopausal status and pelvic

floor dysfunction has not previously been evaluated in women. We postulated that differences in GAG composition could be expected. Our study was conducted to analyze the types and amount alterations of GAGs in the vagina and perineal skin in pre- and postmenopausal women, according to genital prolapse stage.

Patients and methods

Forty patients were included, divided into four groups. Group A: 10 premenopausal women in with genital prolapse stage 1, whose ages ranged from 36 to 50 years (mean 40.3); Group B: 10 premenopausal women with genital prolapse stages 2 and 3 whose age range was from 30 to 52 years (mean 44.9); Group C: 7 postmenopausal women with genital prolapse stage 1, whose ages ranged from 50 to 71 years (mean 61); Group D: 13 postmenopausal women with genital prolapse stages 2 and 3, whose age range was from 52 to 76 years (mean 65.9). Between August 2001 and July 2002 all patients underwent incontinence surgery, pelvic organ prolapse surgery, or abdominal or vaginal hysterectomy for benign gynecological conditions . Subjects were excluded if they had known connective tissue diseases, diabetes, vulvovaginal infections, or if they were smokers. Those who had used estrogen, progestogens and androgens in the previous 12 months were not included. All patients underwent a standard physical examination that included Pelvic Organ Prolapse Quantification (POP-Q) according to the standardization of the terminology of female pelvic organ prolapse [7]. The stage of prolapse in the posterior compartment was determined by measured of the upper posterior vagina wall (Bp point).

During the surgical procedure, full-thickness samples were removed from the posterior vaginal wall in the midline (upper one-third, 1–2 cm from the uterine cervix) measuring roughly 5 mm in diameter, and from the midline skin of the perineal body, beyond the introitus, also measuring roughly 5 mm in diameter. The tissues were obtained with Metzenbaum scissors. The vaginal wall samples were 3–4 mm in depth and included vaginal epithelium, subepithelial and connective tissue. The skin samples included dermis and epidermis, but not scar tissue from prior episiotomies or laceration repairs. Each patient only received one biopsy from each site and there were no complications. All patients gave their informed consent to participate in this study, and the Local Ethics Committee approved its protocol.

Isolation and fractionation of glycosaminoglycans

Immediately after resection, each sample was rinsed in cold phosphate-buffered saline (PBS) solution to remove excess blood. Afterwards, the specimen was weighed and maintained in 10 volumes of acetone. After standing overnight at room temperature, the dry tissue powder was incubated overnight with maxatase (3 mg/ml in 0.06 M phosphate-cysteine buffer, pH 6.5, containing 20 mM EDTA) at 50ºC. Trichloroacetic acid 90% and sodium chloride were added to the supernatant up to 10% and 1 M final concentrations, respectively. The mixture was left to stand for 10 min at 4ºC and the precipitate formed was removed by centrifugation at 4000 *g* for 20 min. The GAGs were precipitated from the supernatant by the slow addition of two volumes of methanol with shaking. After 18–24 h at −20ºC the precipitate was collected by centrifugation, vacuum dried, resuspended in 0.5 ml of a solution containing desoxyribonuclease-I (1 mg/ml) and 0.05 M sodium acetate buffer, 0.02 M magnesium chloride, pH 5.0, and incubated at 30ºC for 18 h. GAGs were analyzed by agarose gel electrophoresis 8 (100 V for 2 h) at 4ºC. After electrophoresis, GAGs were precipitated in gel with 0.1% cetyltrimethylammonium for 2 h. The agarose gel strips were stained with 0.1% toluidine blue in 1% glacial acetic acid and 50% ethanol. The relative concentration of GAGs was determined by densitometry of toluidine blue-stained gel using a Hewlett-Packard spectrophotometer with a wavelength of 525 nm. The three peaks obtained were identified as chondroitin sulfate, dermatan sulfate and heparan sulfate using previously described procedures [8].

Statistical analysis

Results are expressed as the mean ± standard deviation (SD) for continuous variables. Statistical comparisons between groups were conducted by Student's *t*-test for normally distributed data or $\chi 2$ tests for categorical variables. Comparisons between multiples groups of total GAGs, CS, DS and HS amounts were conducted by one-way analysis of variance (ANOVA), followed by the Tukey multiple comparisons test. The relative concentration of total sulfated glycosaminoglycans, DS, HS and CS was compared between the samples inside each group with *t*-test for paired samples. A p value of < 0.05 was considered significant.

Results

A total of 40 patients were analyzed. Clinical data of patients with respect to age, parity and body mass index are listed in Table 1. Sulfated glycosaminoglycans were analyzed by agarose gel electrophoresis (Fig. 1).

Vaginal tissue and perineal skin showed three different types of GAGs. In general, the predominant type was DS, accounting for 85% of the total, followed by CS and HS (Fig. 2). The amount of DS in vaginal tissue and perineal skin from each studied group was significantly greater than the amount of CS ($p < 0.001$) and HS ($p < 0.0001$) by Student's *t*-test. The amounts of CS and HS did not vary significantly.

Table 1 Clinical data of general features of the patients by menopausal status. Values are given as mean ± standard deviation. Independent samples *t* -test for differences between age, parity and body mass index

	Pre-menopause ($n=20$)	Post-menopause ($n=20$)	p value
Age (yrs)	42.6 ± 5.8	64.2 ± 7.9	< 0.0001
	A group: 40.3 ± 3.9	C group: 61.0 ± 6.8	A x B: 0. 07
	B group: 44.9 ± 6.6	D group: 65.9 ± 8.2	C x D: 0. 19
Parity	4.5 ± 3.07	3.9 ± 3.1	0.54
Body mass index	26.4 ± 4.2	29.5 ± 4.8	0.06

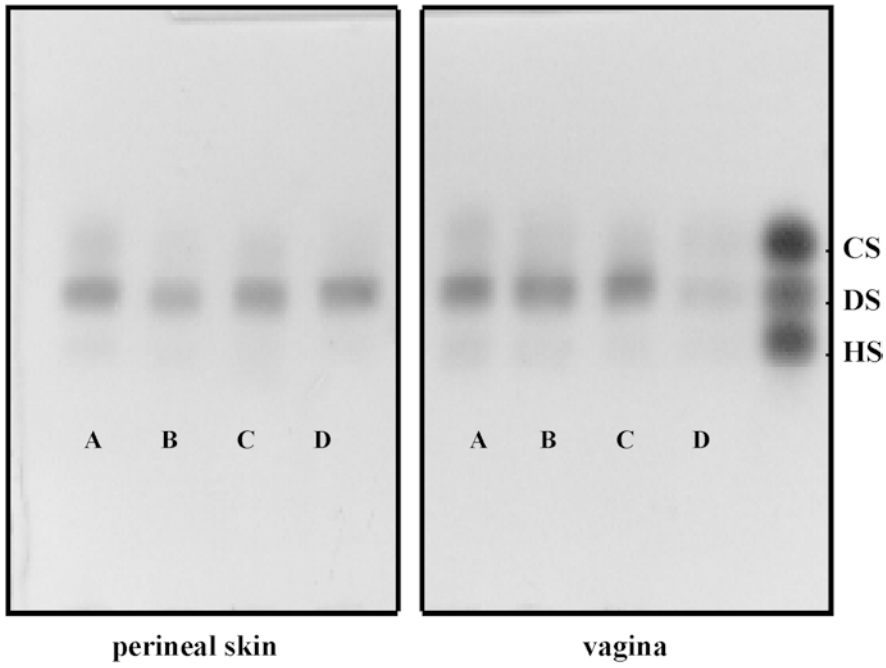

Fig. 1 Agarose gel electrophoresis of GAGs of vaginal tissue and perineal skin yielded three bands. The fastest migrating band had mobility similar to that reference chondroitin sulfate (*CS*). The middle band had mobility similar to that of reference dermatan sulfate (*DS*), and the third band was similar to heparan sulfate (*HS*). The GAGs were quantified by densitometry (525 nm) of the agarose gel slabs (not demonstrated). The *CS*, *DS* and *HS* contents clearly decreased in the *C* and *D* groups. *A*: premenopause group with prolapse stage 1; *B*: premenopause group with prolapse stage 2 and 3; *C*: postmenopause group with prolapse stage 1 and *D* postmenopause group with prolapse stage 2 and 3

In posterior vaginal wall tissue total GAGs, DS and HS concentrations in postmenopausal women with prolapse stages 2 and 3 were significantly decreased compared to premenopausal women with prolapse stage 1 ($p < 0.01$; $p < 0.01$; $p < 0.001$, respectively) and premenopausal women with prolapse stage 2 and 3 ($p < 0.001$; $p < 0.01$; $p < 0.05$, respectively), and, finally, compared to postmenopausal women with prolapse stage 1 ($p < 0.05$; $p < 0.05$; $p < 0.05$, respectively). However, there were no significant differences in CS in postmenopausal women with prolapse stage 2 and 3 when compared to the postmenopausal group with prolapse stage 1. However, CS concentration in the vagina of postmenopausal women with prolapse stages 2 and 3 was significantly decreased compared to the premenopausal group with prolapse stage 1 ($p < 0.01$) and premenopausal group with prolapse stages 2 and 3 ($p < 0.05$). Finally, CS in postmenopausal women with prolapse stage 1 was significantly decreased compared to the premenopausal group with prolapse stage 1 ($p < 0.01$) (Table 2 and Fig. 2).

In perineal skin the amounts of total GAGs, DS and HS did not vary significantly in pre- and postmenopausal women, according to genital prolapse stage. However, CS concentrations in postmenopausal women with prolapse stage 1 and prolapse stages 2 and 3 were significantly decreased compared to women in premenopausal with prolapse stage 1 ($p < 0.01$) (Table 3 and Fig. 3).

Discussion

GAGs have been previously studied in different tissues and implicated in genitourinary diseases and leiomyoma [9, 10, 11, 12]. However, studies linking GAGs and genital prolapse to menopausal status have not yet been carried out. The use of vaginal epithelium in the study of pelvic organ prolapse is common [1, 2]. The major finding of this investigation is that the amount of GAGs in the posterior vaginal wall is diminished in postmenopausal women with advanced stages of genital prolapse.

In our study the sulfated glycosaminoglycans found were dermatan sulfate (DS), chondroitin sulfate (CS) and heparan sulfate (HS). DS was also the one with the highest expression. CS and HS were also found in much lower quantities in almost all samples. H However, they did not show significant differences between them in the groups studied. Our data are consistent with what has

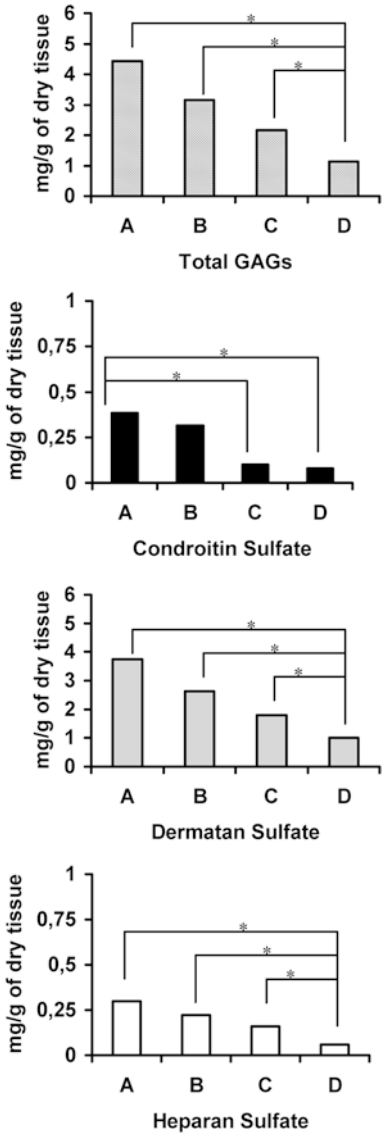

Fig. 2 Relative concentration of GAGs in four groups of vaginal tissue. Premenopause group with prolapse stage 1 (*A*) and with prolapse stage 2 and 3 (*B*), postmenopause group with prolapse stage 1 (*C*) and with prolapse stage 2 and 3 (*D*). CS = chondroitin sulfate; DS = dermatan sulfate and HS = heparan sulfate. Values are expressed as milligrams of glycosaminoglycan per gram of dry tissue. We observed a significant reduction of sulfated glycosaminoglycans in vaginal tissue from premenopausal women to postmenopausal, according to genital prolapse stage. Comparisons between multiple groups were conducted by a one-way analysis of variance (ANOVA) followed by the Tukey multiple comparisons test. * indicates $p < 0.05$

been observed in studies with other types of human tissue, e.g. male spongy urethra [13] and normal myometrium [12].

We found significant differences between GAGs in vaginal tissue. The total amounts of GAG, CS, DS and HS in premenopausal women with prolapse stage 1 and prolapse stages 2 and 3 were significantly higher than in postmenopausal patients with prolapse stages 2 and 3. However, we did not observe differences in premenopausal women in the total amount of GAGs, CS, DS and HS of the vaginal tissue and perineal skin in patients with prolapse stage 1 compared to those with prolapse stages 2 and 3.

Table 2 Means (± standard deviation) of total sulfate glycosaminoglycans, chondroitin sulfate, dermatan sulfate and heparan sulfate in four groups of vaginal tissue (values are expressed as milligrams of glycosaminoglycan per gram of dry tissue)

mg/g tissue	Group A $n=10$	Group B $n=10$	Group C $n=07$	Group D $n=13$
GAGs	4.43 ± 3.25	3.16 ± 1.5	2.16 ± 1,01	1.13 ± 0.81
CS	0.38 ± 0.32	0.31 ± 0.27	0.1 ± 0.07	0.07 ± 0.08
DS	3.74 ± 2.91	2.62 ± 1.34	1.8 ± 0.86	0.99 ± 0.7
HS	0.29 ± 0.19	0.22 ± 0.24	0.15 ± 0.01	0.03 ± 0.04

GAGs: total sulfated glycosaminoglycans; DS: dermatan sulfate; CS: chondroitin sulfate; HS: heparan sulfate
ANOVA = variance analysis; CI = confidence interval
Significant differences:
Total GAGs
> ANOVA (AxBxCxD): F: 5.99, $p=0.002$
Tukey's multiple comparison test: (A = B, A = C, A > D, B = C, B > D, C > D)
CS
ANOVA (AxBxCxD): F: 5.08, $p=0.004$
Tukey's multiple comparison test: (A = B, A > C, A > D, B = C, B > D, C = D)
DS
ANOVA (AxBxCxD): F: 5.32, $p=0.003$
Tukey's multiple comparison test: (A = B, A = C, A > D, B = C, B > D, C > D)
HS
ANOVA (AxBxCxD): F: 4.25, $p< 0.05$
Tukey's multiple comparison test: (A = B, A = C, A > D, B = C, B > D, C > D)

Table 3 Means (± standard deviation) of total sulfate glycosaminoglycans, chondroitin sulfate, dermatan sulfate and heparan sulfate in four groups of in perineal skin (values are expressed as milligrams of glycosaminoglycan per gram of dry tissue)

mg/g tissue	Group A $n=10$	Group B $n=10$	Group C $n=07$	Group D $n=13$
GAGs	2.47 ± 0.94	1.63 ± 0.88	1.74 ± 1.31	1.65 ± 1.49
CS	0.16 ± 0.14	0.05 ± 0.05	0.03 ± 0.05	0.03 ± 0.02
DS	2.02 ± 0.69	1.39 ± 0.71	1.49 ± 1.33	1.4 ± 1.35
HS	0.28 ± 0.15	0.18 ± 0.16	0.06 ± 0.04	0.13 ± 0.23

GAGs: total sulfated glycosaminoglycans; DS: dermatan sulfate; CS: chondroitin sulfate; HS: heparan sulfate
ANOVA = variance analysis; CI = confidence interval
Significant differences:
Total GAGs
ANOVA (AxBxCxD): F: 0.95, $p=0.042$
Tukey's multiple comparison test: (A = B, A = C, A = D, B = C, B = D, C = D)
CS
ANOVA (AxBxCxD): F: 4.51, $p=0.009$
Tukey's multiple comparison test: (A = B, A > C, A > D, B = C, B = D, C = D)
DS
ANOVA (AxBxCxD): F: 0.68, $p=0.57$
Tukey's multiple comparison test: (A = B, A = C, A = D, B = C, B = D, C = D)
HS
ANOVA (AxBxCxD): F: 2.14, $p=0.11$
Tukey's multiple comparison test: (A = B, A = C, A = D, B = C, B = D, C = D)

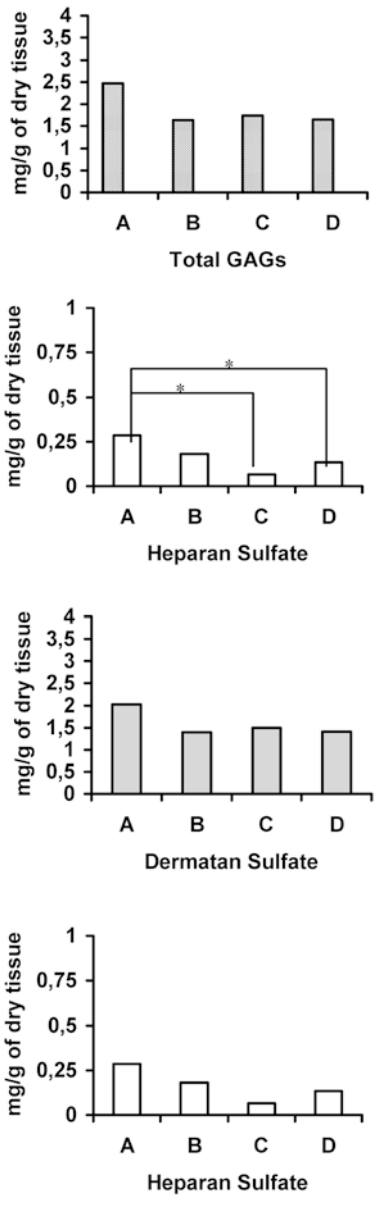

Fig. 3 Relative concentration of GAGs in four groups of vaginal tissue. Premenopause group with prolapse stage 1 (*A*) and with prolapse stage 2 and 3 (*B*); postmenopause group with prolapse stage 1 (*C*) and with prolapse stage 2 and 3 (*D*). CS = chondroitin sulfate; DS = dermatan sulfate and HS = heparan sulfate. Values are expressed as milligrams of glycosaminoglycan per gram of dry tissue. Except for CS, we did not observe a significant reduction in sulfated glycosaminoglycans in perineal skin from premenopausal women to postmenopause, according to genital prolapse stage. Comparisons between multiple groups were conducted by a one-way analysis of variance (ANOVA), followed by the Tukey multiple comparisons test. * indicates $p < 0.05$

We observed a significant decrease in total GAG values, DS and HS, in the postmenopausal group, between the women with prolapse stages 2 and 3 and those with stage 1, but not in the amount of CS. We found a significant decrease of CS only in vaginal tissue inpremenopausal women with prolapse stage 1, and postmenopausal patients with prolapse stage 1. Maybe the postmenopausal state alone can account for the CS decrease. We did not find significant differences between GAGs in perineal skin regarding the amounts of DS and HS. However, the amount of CS in menacme patients with prolapse stage 1 was significantly higher than that of postmenopausal patients with prolapse stage 1 and stages 2 and 3.

It is important to emphasize that, when comparing pre- and postmenopausal patients, there was obviously a significant difference regarding age. Therefore, we cannot draw conclusions in our study regarding hypoestrogenism entirely, without referring to the tissue alterations inherent to the aging process.

This is a preliminary study and we acknowledge that there are some limitations. There is a small sample size and, because of ethical limitations, we did not have an ideal control group consisting of women with no afflictions. The second limitation is that the study examined patients after they have already had a clinical disorder develop. This is not a prospective study that has followed up women across time to make measurements before and after a disorder has developed. We therefore cannot be sure of the direction of any effects we see; it may be that a change in GAGs causes the development of genital prolapse, or it may rather be that genital prolapse causes changes in GAG metabolism or production as some secondary compensatory effect. Future well-designed studies in humans will be necessary to define the precise relationship between vaginal GAG content, estrogen and prolapse.

It is possible that the higher reduction in total GAGs, CS, DS, and HS found in the vagina of postmenopausal women is due to a response to tissue injury of the ECM (which had undergone successive trauma due to childbirth) combined with the effects of hypoestrogenism. Previous studies in human skin showed a decrease in GAGs according to age, being evident for HS as well as for DS [14]. In animal models, there was a total GAG reduction in the skin of adult rats compared to young rats [15]. The castration of female adult rats reduced GAG content in the bladder, and therapy with conjugated estrogens and medroxyprogesterone acetate increased the GAG content to values similar to those of non-castrated rats [16].

DS chains are found in low molecular weight proteoglycans (decorin and biglycan). They interact with collagen relating to the organization, fibril deposition velocity and stabilization, guiding fibrilogenesis [17]. In vaginal tissue the decrease of DS in the postmenopausal period seems to correlate with findings in the literature on increased collagenolytic activity, the disarray of collagen fibers, and alterations in their solubility and thickness in patients with pelvic floor dysfunction [1, 18, 19].

HS and heparin bind to several growth factors, such as interleukins 3, 4 and 8, FGF, TGF-β and PDGF, among others [12]. Collagen biosynthesis is, for example, stimulated by some growth factors connected to HS. A decreased in HS expression or a decrease in its

biosynthesis would reduce the tissue availability of growth factors in ECM and inhibit tissue growth and differentiation [5].

CS is an inhibitor of extracellular proteases involved in the metabolism of connective tissue. It increases the anabolic activity and limits the excessive degradation of ECM. Thus, it can act as a structural modulator, maintaining the integrity of the intercellular space [20]. Thus, the decrease of CS can be related to the increase in its proteases, with a consequently higher degradation and disarray of ECM components.

Finally, we hypothesized that, in general, there is an additive effect between postmenopausal state and genital prolapse that may be associated with the decrease in amount of GAGs in genital tissue. GAGs contribute to the physical properties of tissues and are involved in tissue resistance and elasticity [21]. Owing to the interaction with other ECM components, it could be suggested that GAGs have a key role in resistance and compliance of the pelvic supporting structures. In fact, the ultrastructural processes that influence these changes in the vaginal wall during the pathogenesis of pelvic organ prolapse are not known. The clinical relevance of these changes seems to be a considerable impairment of the mechanical properties of the tissue. Therefore, prospective longitudinal studies are needed to better clarify the role of the pathophysiological factors involved.

References

1. Jackson SR, Avery NC, Tarlton JF, Eckford SD, Abrams P, Bailey AJ (1996) Changes in metabolism of collagen in genitourinary prolapse. Lancet 347:1658–1661
2. Takano CC, Girão MJBC, Sartori MGF et al. (2002) Analysis of collagen in parametrium and vaginal apex of women with and without uterine prolapse. Int Urogynecol J 13:342–345
3. Liapis A, Bakas P, Pafti A, Frangos-Plemenos M, Arnoyannaki N, Creatsas G (2001) Changes of collagen type III in female patients with genuine stress incontinence and pelvic floor prolapse Eur J Obstet Gynecol Reprod Biol 97:76–79
4. Ruggeri A, Motta PM, eds. (1984) Ultrastructure of the connective tissue matrix. Martinus Nijhoff, Boston
5. Kjellen L, Lindahl U (1991) Proteoglycans: structure and interactions. Annu Rev Biochem 60:443–475
6. Iozzo R (1998) Matrix proteoglycans: from molecular design to cellular function. Annu Rev Biochem 67:609
7. Bump RC, Mattiasson A, Bo K et al. (1996) The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 175:10–17
8. Nader HB, Ferreira TM, Paiva JF et al. (1984) Isolation and structural studies of heparan sulfates and chondroitin sulfates from three species of molluscs. J Biol Chem 259:1431–1435
9. Wlodavsky I, Korner G, Ishai-Michaeli R, Bar-Shavit R, Fuks R (1990) Extracellular matrix-resident growth factors and enzymes: possible involviment in tumour metastasis and angiogenesis. Cancer Metastasis Rev 9:203–226
10. Russel AL (1999) Glycosaminoglycan deficiency in protective barrier as an underlying primary cause of ulcerative colitis, Crohn's disease, intersticial cystitis and possibly Reiter's syndrome. Med Hypotheses 52:297–301
11. Wegrowski Y, Bellon G, Quereux C, Maquart FX (1999) Biochemical alterations of uterine leiomyoma extracellular matrix in type IV Ehlers-Danlos syndrome. Am J Obstet Gynecol 180:1032–1034
12. Wolanska M, Sobolewski K, Drozdzewicz M, Bankowski E (1998) Extracellular matrix components in uterine leiomyoma and their alteration during the tumour growth Mol Cell Biochem 189:145–152
13. Silva EA, Sampaio FJB, Ortiz V, Cardoso LEM (2002) Regional differences in the extracellular matrix of the human spongy urethra as evidenced by the composition of glycosaminoglycans. J Urol 167:2183–2187
14. Carrino DA, Sorrell JM, Caplan AI (2000) Age-related changes in the proteoglycans of human skin. Arch Biochem Biophys 373:91–101
15. Merle B, Durussel L, Delmas PD (1999) Decorin inhibits cell migration through a process requiring its glycosaminoglycans side chain. J Cell Biochem 75:538
16. De Deus JM, Sartori MGF, Girão MJBC et al. (2004) Glycosaminoglycan profile in bladder and urethra of castrated rats treated with estrogen, progestogen and raloxifen. Am J Obstet Gynecol (in press)
17. Iozzo RV (1997) The family of small leucine rich proteoglycans: key regulators of matrix assembly and cellular growth. Crit Ver Biochem Mol Biol 32:141–174
18. Chen BH,Wen Y, Li H, Polan ML (2002) Collagen metabolism and turn over with stress urinary incontinence and pelvic prolapse. Int Urogynecol J 13:80–87
19. Fitzgerald MP, Mollenhuer S, Benson JT, Brubaker L (2000) Urethral collagen morphologic characteristics among women with genuine stress incontinence. Am J Obstet Gynecol 18:1565–1574
20. Bayliss MT, Osborne D, Woodhouse S, Davidson C (1999) Sulfation of chondroitin sulphate in human articular cartilage. The efect of age, topographical positon, and zone of cartilage on tissue composition. J Biol Chem 274:15892–15900
21. Wight TN, Neinegard DK, Hascall VC (1991) Proteoglycans structure and function. In: Hay ED, ed. Cell biology of extracellular matrix, 2nd edn. New York, Plenum Press, pp.45–78

Editorial comment

The role of connective tissue metabolism in the pathophysiology of pelvic organ prolapse is poorly understood. This study noted that the posterior vaginal wall of postmenopausal women with pelvic organ prolapse had significantly less extracellular matrix sulfated glycosaminoglycans than in premenopausal women with pelvic organ prolapse. The study's limitations include lack of a control group, and small sample size. Ideally, women should be followed prospectively to see if these cellular changes truly coincide with the development of prolapse.