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IS INCREASED COLLAGEN METABOLISM THE CAUSE OR EFFECT OF PROLAPSE?: A CONTROLLED STUDY

Aims of Study

There is a 11.7% risk during a lifetime of having at least one operation for genital prolapse (1). Risk factors include childbirth, ageing, menopause and connective tissue disorders (2). Collagen metabolism is altered in the vaginal skin of women with genitourinary prolapse. Jackson et al. (3), showed a significant reduction in the collagen content and increase in the matrix metalloproteinases (MMP2 and MMP9), suggesting an up regulation of collagen breakdown and remodelling. He postulated this as a cause of prolapse but did not prove wether this is cause or effect. The aim of this study was to compare collagen metabolism by measuring MMP2 expression in stretched and non-stretched vaginal tissue from women with prolapse allowing them to be their own controls. This would allow us answer the question of cause and effect.

Methods

Based on previous tissue studies a minimum of 9 patients was required to allow a 90% power calculation to detect a difference at 0.05 significance level. Eleven women presenting with vaginal prolapse repair were included in the study after ethical committee approval and informed consent. Patients were booked for cystocele and/or rectocele repair. Tissue samples were obtained at the time of surgery and immediately stored in liquid nitrogen until required for assay. Two samples from the same vaginal wall were obtained for each woman. One was obtained from the excised redundant vaginal skin after plication of the fascia, while the second sample was obtained from tissue proximal to the area repaired but not affected by the prolapse. The latter skin had not been stretched by the prolapsing organ and still contained the folds of normal vaginal skin. Samples were thus divided into two appropriate groups, 'stretched' and 'non-stretched' skin. Tissue samples were homogenised and homogenates were assayed for total protein and MMP2. MMP2 was measured by enzyme immunoassay using a Biotrak MMP2, human, ELISA system kit (Amersham Pharmacia Biotech). This assay recognises the precursor of MMP2 (pro-MMP2), i.e. free pro-MMP2 and that complexed with TIMP2. InStat was used to perform t test and linear regression analysis.

Results

The eleven women had a mean age of 58 years old. We found when compared all samples a significant increase (p = 0.02) in the MMP2 per unit weight in the 'stretched' tissue compared with the matched 'non-stretched' tissue.However there was no significant diference (p=0.92) on the MMP2 per unit of protein in both groups.
In addition, there was a correlation (p= 0.02) between the amount of MMP2 per unit of protein in the 'stretched' tissue compared with the 'non-stretched' tissue of the same women.

Paired t test	stretched	non-stretched	p value
weight	29.18	29.81	p= 0.57
MMP2/weight	**0.15**	**0.11**	**p= 0.02**
MMP2/prot	19.69	19.82	p= 0.92

Linear regression	stretched	non-stretched	p value
MMP2/prot	**19.69**	**19.82**	**p= 0.02**

Conclusions

1. There is a significant increase in MMP2 production in 'stretched' vaginal tissue compared with that which had not undergone any stretching in the same women with vaginal prolapse. That would suggest stretching cuases up regulation.

2. In addition, however, a correlation between MMP2 per unit protein from the stretched tissue matched with the non-stretched of the same women was still seen. This could suggest some inherent factor within the tissue (may be inherited) that leads to up regulation in women with prolapse.

References

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