

IS PROLAPSE RELATED TO CHANGES IN MUSCLE AND CONTENT WITHIN THE VAGINAL EPITHELIUM OR JUST TO A REDUCED VAGINAL THICKNESS?

Hypothesis / aims of study

Vaginal prolapse is associated with changes in total collagen content, solubility and turnover in the vaginal epithelium [1]. It has also been suggested that there are histological variations between different areas of a prolapsed vagina and this would support the fascial defect theory in the pathogenesis of prolapse. Analysis of vaginal epithelium is limited as most studies have examined tissue obtained during surgical procedures which are often not full thickness and from a few sites.

The aim of this study was to compare the muscle to collagen composition at 6 specific locations in the vaginal wall in tissue samples taken from cadavers of women with pelvic organ prolapse and to compare these findings to samples taken from cadavers of women with no pelvic organ prolapse.

Study design, materials and methods

Female cadavers were used as they allowed full thickness biopsies to be taken. The cadavers had been fixed in the standing position using a formaldehyde based solution. The fluid was pumped into the cadavers at high pressure accentuating any prolapse to then become apparent. Once the cadavers were fixed POP-Q measurements were performed in the supine position. The cadavers were then classified as having prolapse if the measurements were greater or equal to stage 2 prolapse. Prolapse was felt to be absent if the measurements were stage 1.

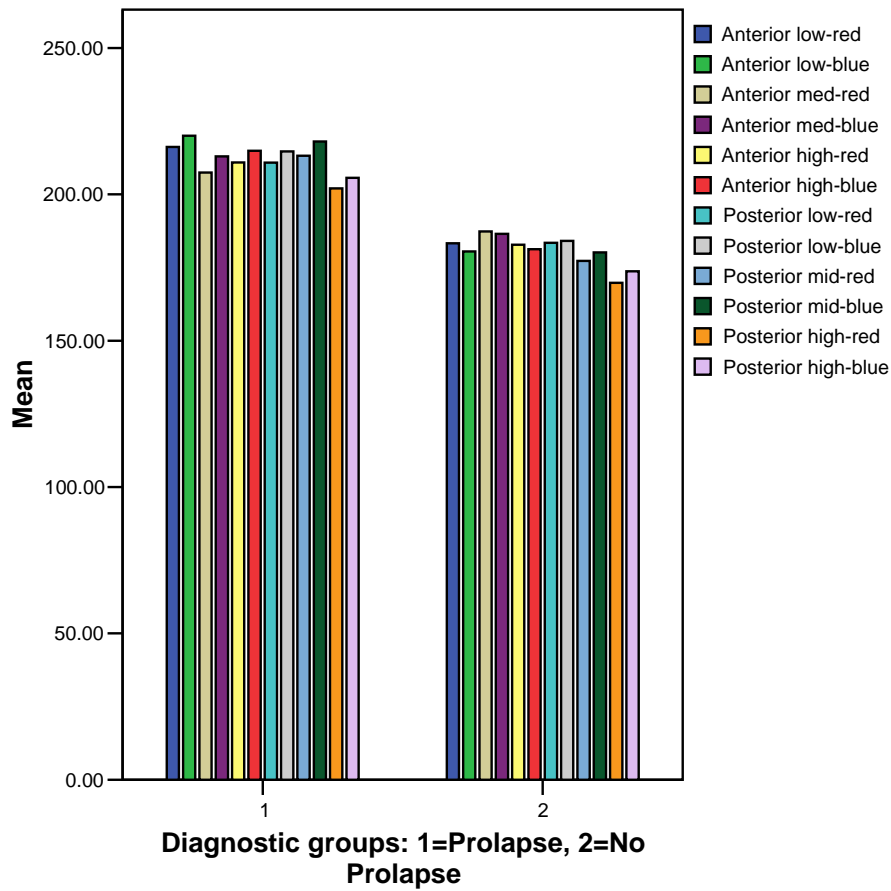
Biopsies were taken from 6 specific locations in the vagina, 3 from the anterior wall, caudal (A), middle (B) and cranial (C) and 3 from the posterior wall caudal (D), middle (E) and cranial (F). The biopsies involved a full thickness of the vagina through to the lumen of the bladder, rectum or peritoneum depending on the position of the biopsy. Masson trichrome stain was used to determine the distribution of muscle and collagen just under the epithelial layer. All the biopsies were stained in one batch using an automated method to ensure uniform staining of the tissues. The stained sections were analysed using a Nikon Eclipse DXM1200 and an image analysis system (Lucia version 4.60). The image analysis system determines the levels of red, green and blue in the biopsy specimen indicating the relative balance of connective tissue (blue) and muscle (red). Initially the reproducibility of the technique was tested by taking 10 sample areas from 10 specimens. The variance was then calculated to determine the optimal number of sections for reproducible results. Then the specimens were analysed. Both the initial tests for reproducibility and final measurements were carried out without changing the settings on the microscope to prevent introducing bias into the results. The total thickness of the vaginal parts of the biopsies were also measured using the image analysis system to determine whether there were variations in vaginal thickness or differences between those with measured vaginal prolapse and those without.

Results

Specimens were taken from 10 cadavers- 5 with prolapse and 5 without.

There was significantly more muscle found in patients with prolapse compared to controls when sampled low ($p=0.047$) and high ($p=0.028$) on the anterior vaginal wall and low ($p=0.028$) and middle ($p=0.016$) on the posterior wall. There is significantly more collagen in patients with prolapse compared to controls when sampled low ($p=0.016$), mid ($p=0.047$) and high ($p=0.047$) on the anterior wall and low ($p=0.016$) and mid ($p=0.009$) on the posterior wall. There was no significant difference in the ratio of muscle to collagen in patients with prolapse compared to controls.

Fig1: Comparison of muscle and collagen content of biopsy sites between prolapse and non-prolapse subjects.



Interpretation of results

There is significantly more collagen and muscle in patients with prolapse compared to controls in all areas apart from high on the posterior wall. There is no significant difference between the ratios of muscle to collagen at all areas sampled.

Concluding message

This data supports previous data that indicate that there may be differences in protein content in women with prolapse compared to controls [2]. Women with prolapse have been shown to have an over expression of muscle actin and myosin genes, and the findings from our study may support a hypothesis that changes in gene expression in prolapse women may alter the collagen/muscle composition of vaginal tissues and so predispose to prolapse.

References

1. Lancet 1996;347:1658-1661.
2. Am J Obstet Gynecol 2003;189:102-12.