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TITLE: DIFFERENTIAL GENE EXPRESSION IN UTEROSACRAL LIGAMENT AND FULL THICKNESS ANTERIOR VAGINAL TISSUES FROM PATIENTS WITH RECURRENT AND PRIMARY PELVIC ORGAN PROLAPSE

Hypothesis / aims of study

Objective: The objective of this study was to profile differential gene expression in three distinct patient groups. We hypothesised that a differentially expressed gene pattern would be seen in women with recurrent pelvic organ prolapse (POP).

Study design, materials and methods

Our groups consisted of women with recurrent POP, women with primary POP and women without POP. Whole human genome DNA microarray analysis technology was used to test this hypothesis in patients with recurrent POP compared to patients with primary POP and non-prolapse controls. The tissue evaluated was anterior vaginal wall tissue and uterosacral ligament (USL) tissues obtained at the time of each women's primary surgery. This study has undergone Institutional Review Board approval at Sanford Health and also the University of South Dakota. Patients enrolled have provided written informed consent.

Results

Results: The evaluation of vaginal and USL tissues yielded more than 450 genes each found to be differentially expressed by 2 fold or greater. We identified in USL tissue 10 genes of interest. Eight genes were over expressed and two genes were under expressed. Confirmation of degree of gene expression for these ten genes was performed by using the technique of real-time RT-PCR. The vaginal tissues contributed no genes of interest. We found that five of the eight genes which were over expressed functioned in the task of distribution, metabolism or deposition of adipose tissue. The two genes of greatest interest that were under expressed in USL tissue were the HOXD genes D10 and D11. These two genes have been identified in earlier microarray studies as being under expressed in patients with POP.
GeneSpring 7.0 software (Agilent was used to perform ANOVA on the data from statistical analysis of the DNA microarrays; P value set at 0.05. The real-time RT-PCR data was analysis using STAT/SE 9.2 (StataCorp, College Station, TX). We used one way ANOVA, with the assumption that the cycle threshold (Ct) means are normally distributed. We confirmed significance of this data using the non-parametric Kruskal-Wallis test since data normality cannot be confirmed with such small numbers. P value set at 0.05.

Interpretation of results

Conclusions: The most important finding of this study was the identification and recognition of a group of genes found to be over expressed in uterosacral ligament tissue. The function of many of these genes was related to the deposition or differentiation of adipose tissue within USL tissues. This event would be expected to have the effect of weakening this pelvic support structure. The two under expressed HOXD genes seen in the recurrence group only are known to affect change/weakening of the USL's when found to be absent or under expressed.
This project tested the hypothesis that differential gene expression could be used to identify patients with recurrent POP. Indeed, the data showed our hypothesis to be correct.

Concluding message

A larger study that looks at these genes in uterosacral ligament with accompanying histology will be needed to make any additional judgements about results that identify clearly a differential gene expression pattern.

Specify source of funding or grant	**Univ. of South Dakota Grant and OB/GYN Dept. of Medical School**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Sanford Health and Univ. of SD IRB committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**