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ASSOCIATION OF MMP1 PROMOTER VARIANT WITH STRESS URINARY INCONTINENCE AND PELVIC ORGAN PROLAPSE IN WOMEN

Hypothesis / aims of study

Our previous studies have shown increased levels of Matrix Metallo Proteinase -1 activity in the serum and pelvic support tissues of women diagnosed with Stress Urinary Incontinence (SUI) and Pelvic Organ Prolapse (POP). Our study was prompted by a critical lack of information regarding the regulation of MMP-1 expression in women who develop incontinence and POP. There is a variation within the promoter of the MMP-1 gene where the insertion of an extra base (G), 1607 bases up stream of the transcriptional start site, creates an Ets transcriptional enhancer which up regulates MMP-1 expression.

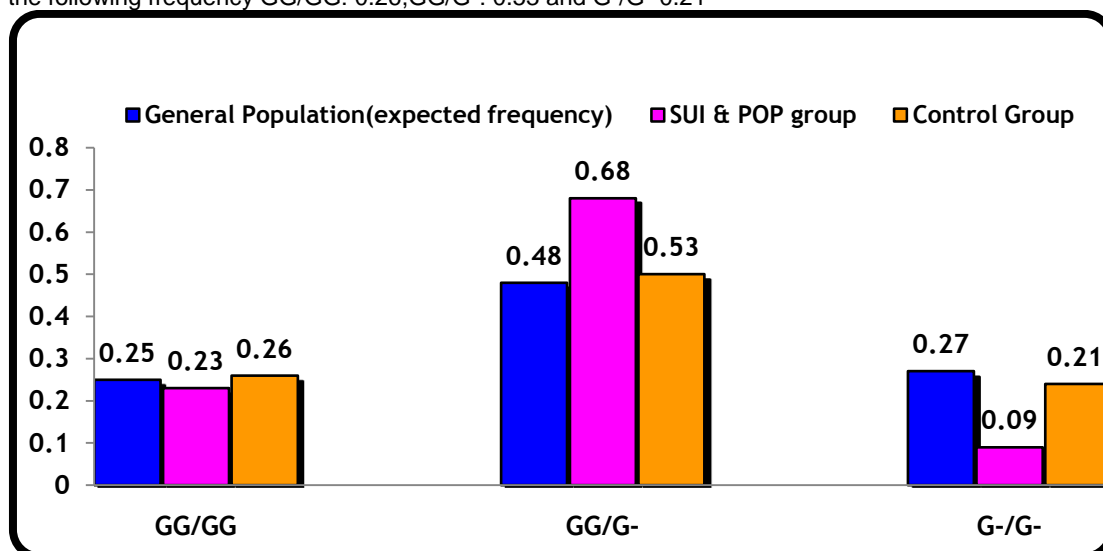
Aim of this study is to determine if the GG promoter genotype of MMP-1 is associated with the increased MMP-1 activity observed in patients with SUI and POP. The expected frequencies of the alleles based on their occurrence within the general population are GG/GG: 0.248, GG/G-: 0.475 and G-/G-: 0.277.

Study design, materials and methods

Fifty-five subjects were enrolled in an IRB approved pilot study. The control group consisted of 15 women without, and the study group of 40 women with, SUI and/or POP. The presence SUI and POP was established by history, physical examination and completion of a validated questionnaire (UDI-6 and IIQ-7). Blood samples were taken, DNA extracted and the promoter region was sequenced. Three primer pair combinations spanning the promoter were used to generate amplicons by PCR. Amplicons for sequencing were recovered from the PCR mixtures and sequenced using the Applied Biosystems big dye Terminator V3.1 cycle sequencing kit. Sequence data was generated using an Applied Biosystems 3130 genetic analyzer. Polymorphisms within the MMP-1 promoter were subsequently identified and recorded.

Results

Of the 55 subjects, 40 had SUI with varying degrees of POP. Thirty six of these patients possessed the GG genotype. Of the 40, 27 were heterozygous possessing both the GG and G- alleles (0.68), 9 were homozygous for the GG allele (0.23), and 4 were homozygous for the G-/G- allele ($p=0.0177$) odds ratio 3.4 with 95% CI 1.17 and 10.14. The control group of 15 patients showed the following frequency GG/GG: 0.26, GG/G-: 0.53 and G-/G-: 0.21



Interpretation of results

Our preliminary data suggests that the frequency of the GG allele in the patient population with SUI and POP significantly exceeds ($p=0.0177$) that of the general population and may explain the increased level of MMP-1 activity previously observed in this patient population

Concluding message

Variations within the promoter region of the MMP1 gene may determine levels of MMP1 expression and explain the differences in MMP1 activity observed in women with and without SUI. At present there is no screening test or diagnostic test to predict the potential to develop SUI and POP.

Specify source of funding or grant	None
Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	Institutional Review Board. IRB Number IRB00005776 Approved 5/29/2008

Was the Declaration of Helsinki followed?

Yes

Was informed consent obtained from the patients?

Yes
