Association of a COL1A1 polymorphism with lumbar disc disease in young military recruits

C Tilkeridis*, T Bei*, S Garantziotis, C A Stratakis

Background: Lumbar disc disease (LDD), one of the most common conditions for which patients seek medical care, has been associated with sequence changes of the COL genes. COL1A1, however, has not been studied in young patients with LDD; COL1A1 polymorphisms have been associated with bone mineral density (BMD) in several populations and with LDD in elderly adults. Objectives: To study COL1A1 polymorphisms in young Greek army recruits with LDD. Subjects: These young soldiers were diagnosed with early LDD at the time of their presentation to a military training site. All patients had radiological confirmation of their disease; a control group was also studied. Methods: Sp1-binding site polymorphism of the COL1A1 gene was investigated by standard methods. Results: There was an increased frequency of the “s” allele in 33.3% in LDD patients; none of the controls had this genotype. In addition, a significantly smaller number of controls was heterozygotes for this allele. Conclusions: A previously studied sequence change of the regulatory region of the COL1A1 gene, the same as has previously been associated with low BMD in many populations and LDD in older adults, showed a strong association with LDD in young male soldiers who were recently diagnosed with this disease.

Table 1 Genotyping data from patients with lumbar disc disease and controls

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Controls (n = 12)</th>
<th>Patients (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G/G</td>
<td>4 (33.3%)</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>G/T</td>
<td>8 (66.7%)</td>
<td>10 (41.7%)</td>
</tr>
<tr>
<td>T/T</td>
<td>0 (0%)</td>
<td>8 (33.3%)</td>
</tr>
</tbody>
</table>

Abbreviations: BMD, bone mineral density; LDD, lumbar disc disease

RESULTS AND DISCUSSION

There was a significant difference between patients with LDD and controls: 33.3% of the patients were T/T vs none of the controls (p<0.001). In addition, a significantly smaller number of controls was heterozygotes for this allele: 66.7% in the LDD patients vs 41.7% in the controls.

T is the “s” allele of the Sp1 binding site COL1A1 polymorphism which has been associated with fractures, low BMD, and BMI. This is the second report of a positive association between the COL1A1 “s” allele and LDD; the first, however, was a study of elderly patients with other bone diseases, in which it was shown that elderly men and women with the TT genotype had a higher risk of disc degeneration than those with the GG and GT genotypes, with an odds ratio of 3.6.

It has been shown that the production of pro-collagen type I increases in LDD, possibly as a repair mechanism. Consistent with this hypothesis, a recent study suggested that collagen type I in a glycosaminoglycan matrix induced
proteoglycans synthesis by canine intervertebral disc cells. In mice genetically engineered for reduced type I collagen, vertebral disc tissue was also mechanically inferior when compared with control animals. It is therefore plausible that an increased ratio of \textit{COL1A1} expression compared with \textit{COL1A2}—as suggested for the effect of this Sp1 binding site polymorphism—may lead to structural alterations as well as to healing defects in the annulus fibrosus and other components of the discs in LDD.

ACKNOWLEDGEMENTS

We thank Dr Joan Marini (NICHD, NIH) for a critical review of this work and submitted text. We also thank Dr Evangelos Kortessas, then Acting Director of the KEYG Center at Arta, Greece, for his support of the study and approval of the research protocol.

Authors’ affiliations

C Tilkeridis*, T Bei*, S Garantziotis, C A Stratakis, Center for Recruitment of Military Personnel for Health Services (KEYG), Hellenic Armed Forces, Arta, Greece, and the Section on Genetics and Endocrinology, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland, USA

*Drs Tilkeridis and Bei have contributed equally to this work and are thus sharing first authorship. Dr Tilkeridis is currently at the Department of Orthopaedics, Demokrition University, Thrace, Greece; Dr Garantziotis is currently at Department of Medicine at Duke University Medical Center, Durham, North Carolina 27710, USA.

Competing interests: none declared

Correspondence to: Dr Constantine A Stratakis, Section on Endocrinology and Genetics, DEB, NICHD, NIH, Building 10, CRC, Room I-3330, 10 Center Drive, MSC 1103, Bethesda, Maryland 20892, USA; stratak@mail.nih.gov

Received 23 March 2005
Revised version received 23 March 2005
Accepted for publication 24 March 2005

REFERENCES