Article Commentary

Evidence update—association between CILP and degeneration of the intervertebral disc: a meta-analysis

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Introduction

Intervertebral disc (IVD) degeneration is an underlying pathological process which leads to lower back pain (1). Whilst initial weakening of IVDs may be asymptomatic, subsequent disc herniation can cause spinal stenosis and segmental instability (2). Conservative or surgical management can alleviate clinical symptoms, but may be unable to prevent continued degeneration.

As degenerative disc disease has been shown to be heritable, studies have analysed associations between IVD degeneration and genetic changes (3-5). Recently, a single-nucleotide polymorphism of the cartilage intermediate layer protein (CILP) gene was identified as a possible etiological factor in IVD degeneration (5). However, there has since been conflicting evidence as to the role of *CILP* gene polymorphism rs2073711 in susceptibility to IVD degeneration (3,5,6). Here we summarise the main study from Wang and colleagues.

Aims

The authors (7) conducted a meta-analysis of case-control and human tissue based studies to determine whether there is an association between CILP polymorphisms and IVD degeneration. The analysis was also subdivided into Asian and European ethnicities to examine heterogeneity between populations.

Search and inclusion criteria

A systematic search of the relevant electronic databases was conducted from their inception to November 2015. Case-control and human tissue based studies investigating the association of CILP polymorphisms and IVD degeneration were included. Search terms including CILP, polymorphism and disc were used to identify these studies. Studies were excluded if they examined disc disease other than degeneration, contained genotype distributions of control samples not in Hardy-Weinberg equilibrium (HWE) or did not have adequate data to obtain odds ratios (ORs) and 95% confidence intervals (CI).

Statistical methods

Data on numbers of controls and cases as well as nations and ethnicities of study populations were recorded. ORs and 95% CIs were also extracted from the studies.

Using STATA version 12.0, the strength of association between CILP polymorphism rs2073711 and IVD degeneration was evaluated by combining ORs and 95% CIs. Heterogeneity between studies was evaluated using Cochran Q and I^2 test. Fixed effects models were used when Q test P value was greater than 0.1 and I^2 was less than 50%, and random effects when above. A subgroup analysis of ethnicity was also performed. Begg's funnel plot and Egger's test were used to assess publication bias, while a sensitivity analysis was performed by withdrawing one study population each time to ensure no single study excessively contributed to the pooled ORs.

Results

Five studies, comprising 1,551 IVD degeneration cases and 1,793 controls, were included. This consisted of four

Asian populations (Japanese and Chinese subjects) and two European populations (Finnish subjects). All study samples conformed to the HWE.

There was no significant heterogeneity between the studies (P=0.165, I^2=36.2%), thus the fixed effects model was used for evaluating any association. It was found that rs2073711 polymorphism was significantly associated with IVD risk (OR =1.36, 95% CI: 1.18–1.55, P<0.001). Subgroup analysis showed a similar OR for both Asian populations (1.35, 95% CI: 1.15–1.55) and European (1.41, 95% CI: 0.99–1.84). Overall heterogeneity was attributed to Asian samples (P=0.074, I^2=56.8%) with no heterogeneity in European samples (P=0.361, I^2=0%). Sensitivity analysis showed that no single study was over responsible for the pooled OR. Finally, no significant publication bias was observed (Begg's test: P=0.133, Egger's test: P=0.256).

Limitations

Whilst there is a strong correlation between CILP polymorphisms and IVD degeneration, the current study was limited by population samples from 3 countries only. More variance in populations is required to demonstrate the effect of ethnicity as the study is underpowered in this regard (8). Furthermore, past studies have shown conflicting results with regards to gender (3,9). However, as most included studies did not include gender-specific association, a gender-specific analysis was not possible in the current study. Finally, the effect of age in the study samples could have a significant impact upon the results.

Implications

The current study has shown CILP gene polymorphism rs2073711 is associated with IVD degeneration. The correlation shown should allow for further research into the molecular mechanisms through which changes in the CILP gene cause IVD degeneration.

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None.

Footnotes

Conflicts of Interest: The authors have no conflicts of interest to declare.

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