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The Relationship between IL-1β [-31 T/C] Gene Polymorphism and Symptomatic Lumbar Disc Herniation

Semptomatik Lomber Disk Hernisi ile IL-1β [-31 T/C] Gen Polimorfizm İlişkisi

Veli CITISLI[1], Aylin KÖSELER[2]

[1]Mugla Sitki Kocman University Medical Faculty, Department of Neurosurgery, Mugla
[2]Pamukkale University Medical Faculty, Department of Biophysics, Denizli

Öz

Bu çalışmada fıtıklaşmış lomber diskte IL-1β [-31 C/T] gen polimorfizmleri arasındaki ilişkinin araştırılması önerilmektedir. IL-1β [-31 C/T] geni PCR [Polimeraz Zincir Reaksiyonu] yöntemi ile amplifiye edildi. Alu I restriksiyon enzimi ile polimorfik site Cut ve genotiplendirme yapıldı. On beş denek (%15), IL-1β geninin -31 konumunda C/C aleli için homozigottu. Kalan 85 denekten 64'ü (%64) C/T için heterozigot ve 21'i (%21) T/T için homozigottu. LDH grubunda on beş denek (%30) IL-1β geninin -31 pozisyonunda T/T alleli için homozigottu. 35 denek C/T için heterozigottu (%70). Kontrol ve LDH grubu arasında önemli farklılıklar vardı. LDH grubunda C/T ve T/T genotipi kontrol grubunagöre daha yüksek, kontrol grubunda ise C/C genotipi daha yüksekti. LDH grubunda C/C genotipi belirlenmedi. Bu çalışmada IL-1β -31T allelinin Lomber herniye disk ile ilişkili olduğu gösterilmiştir

Anahtar Kelimeler: Genotip, IL-1β Polimorfizmi, Lomber Disk Hernisi

Abstract

In this study, the relationship between IL-1β [-31 C / T] gene polymorphisms in the herniated lumbar disc is offered to be investigated. IL-1β [-31 C / T] gene was amplified by the PCR [Polymerase Chain Reaction] method. Polymorphic site cut with the restriction enzyme Alu I and genotyping were performed. Fifteen subjects (15%) were homozygous for the C/C allele at -31 position of IL-1β gene. Of the remaining 85 subjects, 64 (64%) were heterozygous for C/T and 21 (21%) were homozygous for T/T. In LDH group, fifteen subjects (30%) were homozygous for the T/T allele at -31 position of IL-1β gene. 35 subjects were heterozygous for C/T (70%). There were significant differences between control and LDH group. In LDH group, C/T and T/T genotype were higher than the control group, however in control group C / C genotype was higher. C/C genotype was not determined in LDH group. In this study, IL-1β -31T allele is shown to be associated with the Lumbar herniated disc.

Keywords: Genotype, IL-1β Polymorphism, Lumbar Disc Herniation

Introduction

Intervertebral disc degeneration is a suspected cause of common back pain, but both the etiology and pathogenesis of disc degeneration are poorly understood (1-4). Research showed that schmorl nodes of lumbar spine have been found in 16.4% of asymptomatic Southern Chinese (5). Also, another data determined that lumbar disc bulge was observed in 84.8% and disc herniation in 18.2% of asymptomatic Americans older than 55 while less than 10% of Spanish patients with low back pain showed lumbar end plate erosions and spondylolisthesis by MRI (6,7). The prevalence of lumbar disc degeneration is variable in the general population and depends on the individuals studied and their racial background.

Accumulated data support that multifactorial and polygenic condition play an important role on disc degeneration. Twin studies suggested that heredity plays a major role, accounting for an estimated 34–74% of variance in disc degeneration (8).

Variability of human DNA has provided valuable data about the genetic past of human lineages. Analyses of the frequency, variation and distribution of DNA have been used to evaluate current models concerning the process of colonization of the World. It is also important for studies of human pathologies; many studies have shown that DNA polymorphism can play an important role in modulating disease expression (5).

Solovieva et al. investigated polymorphisms within the IL-1 gene locus associated with lumbar disc degeneration (9). Aparicio et al. investigated IL-1β +3953 T/C polymorphism in LDH patients and determined this polymorphism was significantly more frequent among LDH patients compared to controls. So, they concluded IL-1 gene cluster polymorphisms could affect the risk of disc degeneration (10).

Since Interleukin-1beta (IL-1β) is a key pro-inflammatory cytokine, which regulates the expression of several genes involved in inflammation, its clinical significance has been extensively investigated (11, 12). In this study we aimed to investigate IL-1β-31 T/C polymorphism in healthy and disc herniation patients in Denizli province of Turkey.

	ORCID No
Veli CITISLI	0000-0002-1631-3795
Aylin KÖSELER	0000-0003-4832-0436

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Adres / Correspondence : Veli CITISLI
Mugla Sitki Kocman University Medical Faculty, Department of Neurosurgery, Mugla
e-posta / e-mail : velicitisli@mu.edu.tr

Material and Method

Data Collection

Healthy DNA samples (n=100) were taken from individuals. Samples were from unrelated healthy families residing in Denizli province, Turkey. The case group was made of 50 patients, with several clinical symptoms suggestive of LDH and the condition confirmed by Magnetic Resonance Imaging (MRI). LDH symptoms were those described by the Pamukkale University Medical Faculty Neurosurgery Department. This study was approved by the Ethics Committee of Pamukkale University Medical Faculty.

Statistical Analysis

All subjects gave written informed consent forms to participate in the study. Associations between SNP and disease were assessed by Pearson Chi-Square test.

Blood collection and DNA isolation

Blood samples were collected in EDTA vacutainers. DNA was extracted from peripheral blood with the standard phenol chloroform extraction method. DNA amplification primers for the IL-1β -31 site polymorphism were 5′- TCT TTT CCC CTT TCC TTTAAC T -3′ [forward] and 5′- GAG AGA CTC CCT TAG CAC CTA GT -3′ [reverse]. The PCR conditions were as follows: 95°C for 2 min, then 35 cycles of 95°C for 1 min, 60°C for 1 min, 68°C for 1 min, and finally 68°C for 10 min. A fragment containing the AluI [Promega, USA] polymorphic site at position -31 of the IL-1β gene was separated.

Results

Our sample consisted of 100 unrelated individuals. Fifteen subjects (15%) were homozygous for the C/C allele at -31 position of IL-1β gene. Of the remaining 85 subjects, 64 (64%) were heterozygous for C/T and 21 (21%) were homozygous for T/T (Table 1). The frequencies of T and C alleles were 0.53 and 0.47, respectively.

In LDH group, fifteen subjects (30%) were homozygous for the T/T allele at -31 position of IL-1β gene. 35 subjects were heterozygous for C/T (70%) (Table 1). The frequencies of T and C alleles were 0.65 and 0.35, respectively.

Allele and genotype frequencies in cases and controls were compared. There were significant differences between control and LDH group (p=0.013). In LDH group, C/T and T/T genotype were higher than the control group, however in control group C / C genotype was higher. C/C genotype was not determined in LDH group.

Discussion

Previous investigations have found different frequency of IL-1β gene in different population. The present study shows an association between the carriage of the IL-1β [-31 T/C] SNP and symptomatic LDH Turkish patients.

Table 1. Polymorphisms in the cytokines-encoding genes IL-1β -31 T/C in patients with lumbar disc herniation [LDH] and control patients

Control Group[n=100]		LDH Group[n=50]		
-31 T/C [Alu] Genotype [%]		-31 T/C [Alu] Genotype [%]		**P**
C/C	15	C/C	-	0.013
C/T	64	C/T	70	
T/T	21	T/T	30	

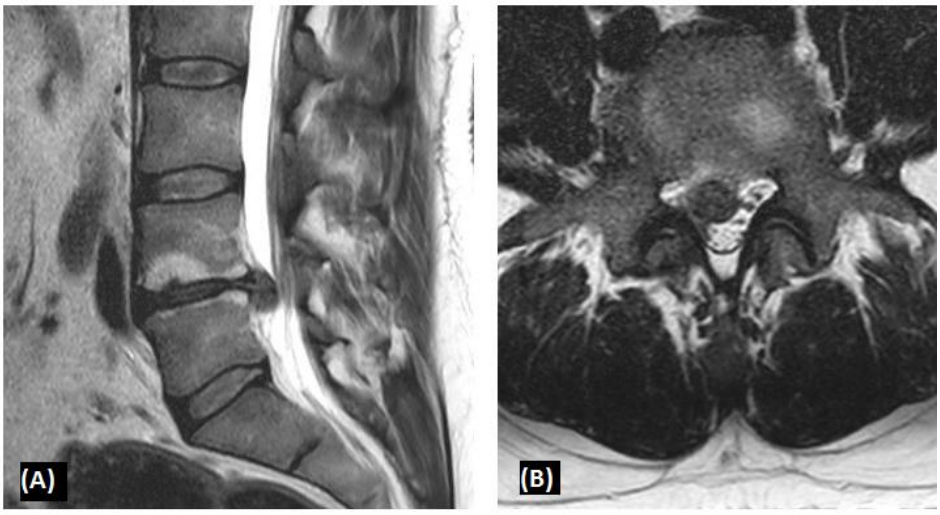

Figure 1. Without-Contrast T2-weighted pre-operative MR images in a 49 -year-old man, who presented with low back pain, right leg pain and neurogenic claudication

Le Maitre et el. showed that IL-1 is produced in the degenerate Intervertebral disc degeneration (13). It is synthesized by native disc cells, and the treatment of human disc cells with IL-1 induces an imbalance between catabolic and anabolic events, responses that represent the changes seen during disc degeneration. Therefore, inhibiting IL-1 could be an important therapeutic target for preventing and reversing disc degeneration (13, 14). Videman et al. examined the allelic diversity of structural, inflammatory, and matrix-modifying gene candidates and their association with disc degeneration. Their data shed light on possible mechanisms of degeneration and support the view that disc degeneration is a polygenetic condition (8). Aparicio et al. studied association of IL-1β +3953 T/C polymorphism and lumbar disc herniation (10). They showed this polymorphism carried by only 8% of LDH patients.

In addition, in a study conducted with Caucasians by Wang et al., it was shown that IL-alpha (+889 C/T) polymorphism was significantly associated with an increased susceptibility to intradiscal disc degeneration (3).

Karppinen et al. found that IL-1 alpha 889C/T polymorphism was correlated with intradiscal disc degeneration in the Finnish population (14).

Chen Y. et al. showed that IL-1 alpha 889 C/T polymorphism was associated with an increased intradiscal disc degeneration in the Chinese population (15).

An analysis of genotype frequency distribution showed that the Indian population differs from the Caucasians with respect to the major genotype at the IL-1β -31 locus. Among Caucasians the major genotype is -31 TT (3, 16).

In a study conducted by Jiang et al. it was found that the IL-1 alpha rs1800587 polymorphism was closely associated with intradiscal disc degeneration in the general population and the IL-1β rs1143684 polymorphism in the Asian population (4).

Rigal et al. showed that disc degeneration is associated with IL-6 rs 1800797 and MMP-9 rs 17576 diseases in the patients with chronic low back pain (17).

We showed the major genotype is -31 T/C, and also C/C genotype was not determined in LDH group. In LDH group, C/T and T/T genotype were higher than the control group, however in control group C / C genotype was higher. Due to the high level of DNA polymorphism observed in populations of different ethnic origin, data on genome variation are widely used in population and evolutionary studies.

In conclusion, these differences may result from the origins of subjects in these studies. In our study all of the subjects were residing in the area of Denizli in which the origins of 30% of the population were Balkan countries. Taken together, these findings raise the possibility that the IL-1β [-31 T/C] genotype distributions within the population living in different regions and/or with different origins may be different. In addition, case and control groups were not matched for age or gender. IL-1β SNP and LDH require further investigation including the determination of serum levels of IL-1β in carriers of this IL-1β SNP, in both LDH cases and controls. Its correlation with other already reported SNPs with intervertebral needs large population studies.

Ethics Committee Approval: Having been approved by the Pamukkale University Ethics Committee with the decision dated 28.11.2018 and numbered 60116787-020/81382.

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