ASSOCIATION OF IL-1beta GENE POLYMORPHISM WITH PROSTHETIC JOINT INFECTION AFTER TOTAL JOINT ARTHROPLASTY

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Introduction

Prosthetic joint infection

Prosthetic joint infection (PJI) can be defined as occurrence of vital bacteria on the prosthetic surface/in the periprosthetic tissues. It is considered a **serious complication** because it requires at least one surgery with removal of the original implant and long-term antibiotics.

Substantial **interindividual variability** observed in PJI frequency suggests contribution of **immunogenetic factors** to host antinfectious immune reactivity.

Cytokines & PJI

Proinflammatory cytokines play an important role namely in innate **immune response** to pathogens potentially causing PJI.

Production and regulation of cytokines is affected by functional variants (**polymorphisms**) of cytokine genes.

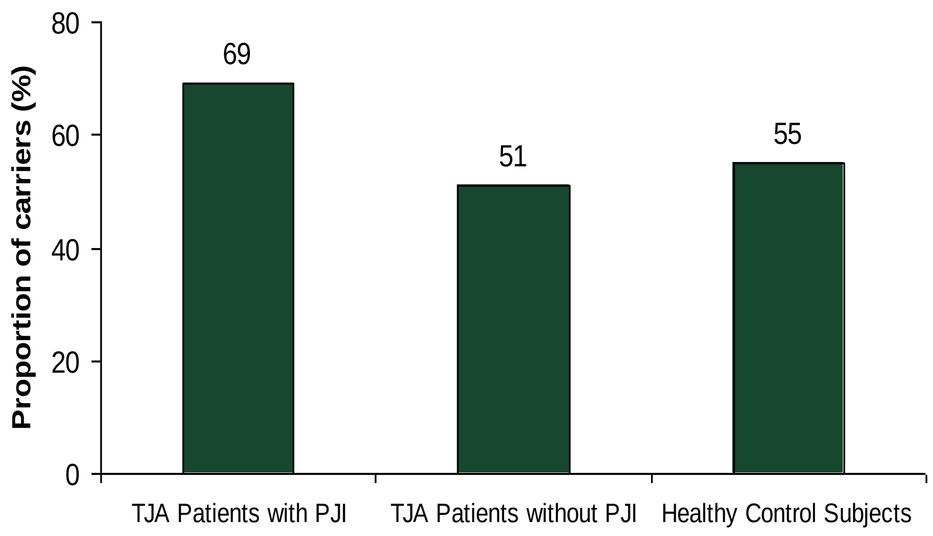
We hypothesized that individual susceptibility /resistance to PJI development is determined by specific combinations of polymorphic markers in cytokine genes**.**

Aim

To determine whether functional gene **polymorphisms in proinflammatory cytokines are associated with PJI after TJA.**

Figure 1: The proportion of the carriers of less common IL1B-511*T allele in the study groups.

TJA – Total Joint Arthroplasty, PJI – Prosthetic Joint Infection



IL1B-511*T carriage rate:

TJA with *versus* without PJI: p=0.006, p_{corr}=0.031; odds ratio=2.06, 95%CI: 1.22-3.47

TJA with PJI *versus* Controls: p=0.04, p_{corr}>0.05; odds ratio=1.76, 95%CI: 1.02-3.02

Conclusion

We nominate a functional variant in the gene encoding cytokine IL-1beta as a possible genetic factor which may contribute to susceptibility to PJI in Czech population.

Our data are of preliminary character and should be independently replicated; possible functional role of IL1B-511 gene variant in PJI remains to be elucidated.

Patients and Methods

Study groups:

Eighty nine patients with PJI after TJA were involved into the study together with two control groups: 1) **TJA control - 214 patients** with TJA that **did not develop PJI** at least 6 yrs. after the surgery, and 2) population control - **168 healthy control subjects** without TJA. All patients/controls were unrelated and of Czech ethnicity.

Genotyping:

Five Single Nucleotide Polymorphisms (SNPs) located in the genes for:

- *Interleukin-1beta (IL1B-511)*
- *Tumour necrosis factor alpha (TNF-308, -238)*
- *Interleukin-6 (IL6-174, nt565)*

Genotyping was performed by PCR–SSP using the “Heidelberg” kit.

Statistical methods:

Distribution of genotypes was tested for conformity with Hardy–Weinberg equilibrium (HWE) using the chi-squared test.

The frequencies of variants were compared between the patients with PJI and both control groups using the standard chi-squared test with Bonferroni correction.

Results

Distribution of genotypes for all investigated polymorphisms conformed to HWE in both control groups; IL-1B-511 genotypes deviated from HWE in the PJI group (p = 0.02).

Observed allele and genotype frequencies and carriage rates for the investigated polymorphisms are summarized in **Table 1**.

The carriers of less common IL1B-511*T allele occurred more frequently among the TJA patients with PJI (69%) **by comparison with the patients that did not develop PJI** (51%, p=0.006, p_{corr}=0.031) **and with healthy control subjects** (55%, p=0.04, p_{corr}>0.05, **Figure 1**).

The distribution of other four investigated cytokine gene polymorphisms did not differ (p>0.05) between investigated study groups (**Table 1**).

Table 1: The genotype and allelic frequencies and carriage rates of five investigated single nucleotide polymorphisms (SNPs) of cytokine genes in 1) patients that developed prosthetic joint infection after total joint arthroplasty (TJA with PJI, N=89), 2) patients without prosthetic infection (TJA without PJI, N=214) and 3) the group of healthy control subjects (N=168). The data are presented as relative values.

	TJA with PJI					TJA without PJI					Healthy Controls				
	Genotype freqs.	Allelic freqs.		Carriage rates		Genotype freqs.	Allelic freqs.		Carriage rates		Genotype frequencies	Allelic freqs.		Carriage rates	
IL1B-511	CC	0.31	C	0.61	C	0.91	CC	0.49	C	0.69	C	0.9	CC	0.45	C	0.68	C	0.91
	CT	0.6					CT	0.42					CT	0.46				
	TT	0.09	T	0.39	T	0.69	TT	0.1	T	0.31	T	0.51	TT	0.09	T	0.32	T	0.55
TNF-308	GG	0.74	G	0.85	G	0.96	GG	0.72	G	0.85	G	0.97	GG	0.68	G	0.83	G	0.98
	GA	0.21					GA	0.25					GA	0.3				
	AA	0.04	A	0.15	A	0.26	AA	0.03	A	0.15	A	0.28	AA	0.02	A	0.17	A	0.32
TNF-238	GG	0.91	G	0.96	G	1	GG	0.93	G	0.96	G	1	GG	0.92	G	0.96	G	1
	GA	0.09					GA	0.07					GA	0.08				
	AA	0	A	0.04	A	0.09	AA	0	A	0.04	A	0.07	AA	0	A	0.04	A	0.08
IL6–174	GG	0.33	G	0.56	G	0.79	GG	0.36	G	0.58	G	0.79	GG	0.33	G	0.58	G	0.84
	GC	0.46					GC	0.43					GC	0.51				
	CC	0.21	A	0.44	A	0.67	CC	0.21	A	0.42	A	0.64	CC	0.16	A	0.42	A	0.67
IL6 nt565	GG	0.34	G	0.57	G	0.8	GG	0.38	G	0.59	G	0.81	GG	0.33	G	0.59	G	0.85
	GA	0.46					GA	0.43					GA	0.52				
	AA	0.2	A	0.43	A	0.66	AA	0.19	A	0.41	A	0.62	AA	0.15	A	0.41	A	0.67

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