Association of Proinflammatory Gene Polymorphisms with Pain-Related Temporomandibular

Zlendić, Marko; Vrbanović, Ema; Tomljanović, Marko; Gall Trošelj, Koraljka; Vuković, Kristina; Alajbeg, Iva

Association of Proinflammatory Gene Polymorphisms with Pain-Related Temporomandibular Disorder

ID 0294

Marko Zlendić[1]*, Ema Vrbanović[1], Marko Tomljanović[2], Koraljka Gall Trošelj[2], Kristina Vuković Đerfi[4], Iva Z. Alajbeg[1,3]

[1] Department of Removable Prosthodontics, University of Zagreb, School of Dental Medicine
[2] Division of Molecular Medicine, Laboratory for Epigenomics, Rudjer Boskovic Institute
[3] University Clinical Center Zagreb, Department of Dentistry
[4] Laboratory for Personalized Medicine, Division of Molecular Medicine, Ruđer Bošković Institute

AIM

This study aimed to investigate the association between single nucleotide polymorphisms (SNPs) in proinflammatory cytokine (*TNF* and *TGFB1*) and chemokine (*CXCL8*) genes with **painful temporomandibular disorders** (TMDp) (Figure 1).

Figure 1.SNP rs2227307 (*CXCL8*) with single nucleotide variants G or T.
(https://www.thermofisher.com/order/genome-database/details/genotyping/C__11748168_10?CID=&ICID=&subtype)

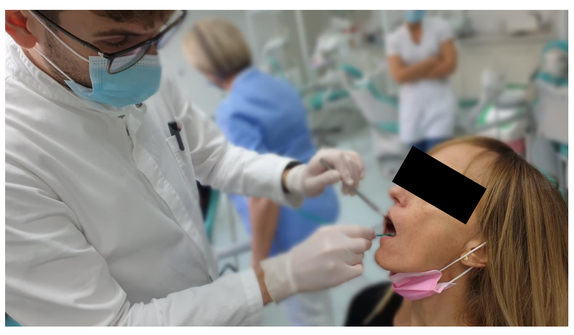

Figure 2. Buccal Mucosa Swabs

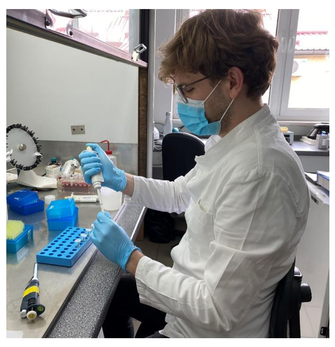

Figure 3. Pipetting DNA Samples for Genotyping

METHODS

Diagnosis of TMDp involves myalgia and/or arthralgia. The study included **170 individuals**: 85 with diagnosed TMDp and 85 healthy controls (CTR). In the TMDp group, the average age was 29.96, with 76 females (89.41%) and 9 males (10.59%). In the control group, the average age was 26.23, with 62 females (72.88%) and 23 males (27.12%).

Intensity of orofacial pain was measured through Characteristic Pain Intensity (CPI) score from **Graded Chronic Pain Scale**, whereas TMD patients with CPI>50 were considered as a high pain intensity group (HPI).

Genomic DNA was extracted from buccal mucosa swabs (Figure 2). Single nucleotide **polymorphisms** (SNPs) in genes encoding **interleukin 8** (*CXCL8;* rs2227306, rs2227307), **transforming growth factor β** (*TGFB1,* rs4803455) and **tumour necrosis factor-alpha** (*TNF*, rs1800629) were analysed by real time-PCR using Taqman Genotyping assays (Figure 3).

The assessment was performed according to dominant and recessive genetic models where minor allele represented the risk allele. Chi-Square Test, Fisher's Exact Test and Mann-Whitney U test were used for data analysis.

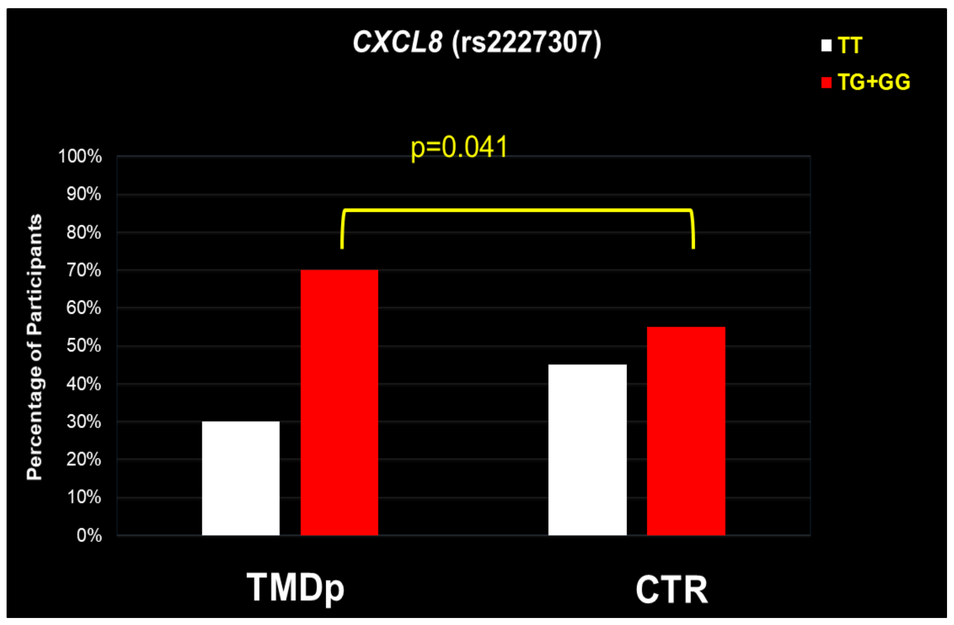

Figure 4. Genotype distribution between Pain-Related Temporomandibular Disorders (TMDp) vs. Controls (CTR) in *CXCL8* (rs2227307)

FUNDING

Croatian Science Foundation Project IP-2019-04-6211 (PI: Iva Alajbeg) and "Young Researchers' Career Development Project - Training of Doctoral Students" (DOK-2020-01) (student: Marko Zlendić).

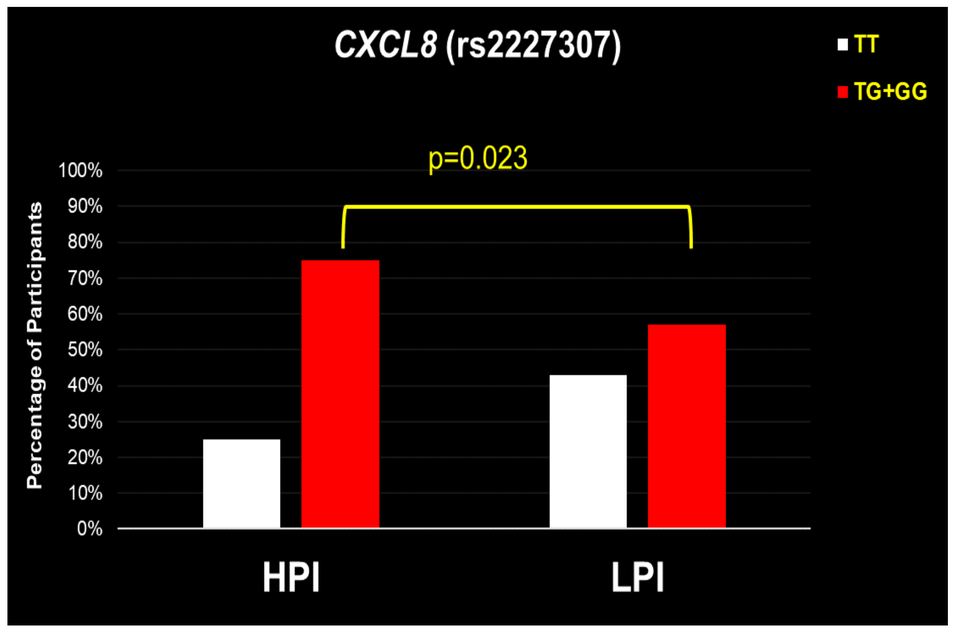

Figure 5. Genotype distribution between patients in high pain intensity (HPI) vs low pain intensity (LPI) group in *CXCL8* (rs2227307)

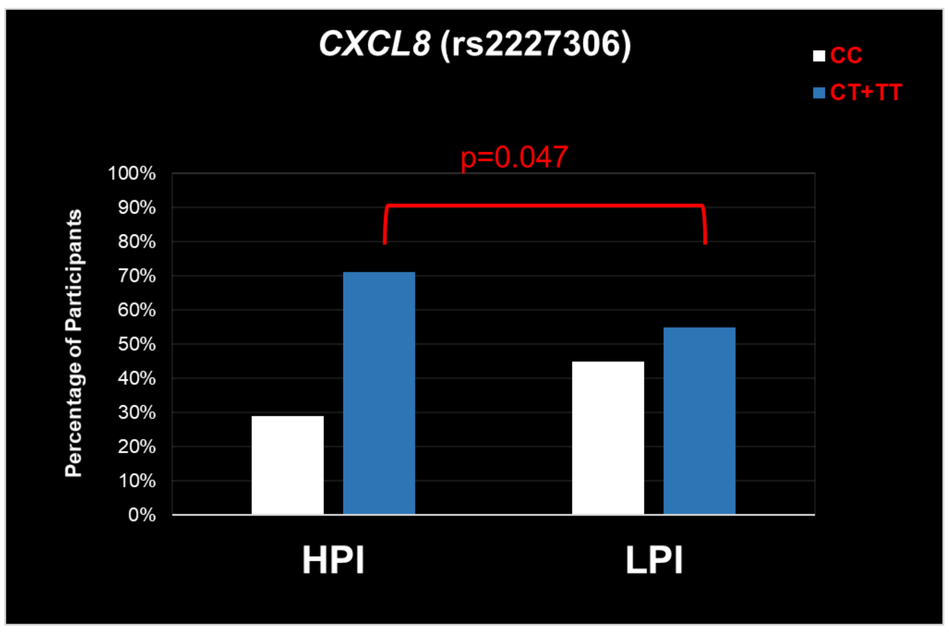

Figure 6. Genotype distribution between patients in high pain intensity (HPI) vs low pain intensity (LPI) group in *CXCL8* (rs2227306)

RESULTS

The frequency of patients carrying **minor allele G of rs2227307** was higher in TMDp patients than in CTRs (70% vs. 55%, p=0.041) (Figure 4).

Carriers of **minor allele G and T of rs2227307 and rs2227306** respectively were significantly more represented in HPI group when compared to the rest of the participants (75% vs. 57%, p=0.023; 71% vs. 55%, p=0.047, respectively) (Figure 5,6).

Also, TMDp subjects carrying **GG+GT of rs2227307** polymorphism reported significantly shorter pain duration in last 6 months (80 vs.112 days, p=0.041) and significantly higher *worst facial pain* (7.3 vs. 6.5, p=0.031) compared to the subjects with the TT genotype.

CONCLUSION

Certain SNPs may predict pain intensity and chronicity in TMDp patients.

Our results support the association between SNPs in pro-inflammatory chemokine genes (*CXCL8*) and TMDp, highlighting the potential utility of genetic testing in predicting pain severity.

Further research is needed to confirm these findings and explore underlying mechanisms.

Marko Zlendić,
dr.med.dent.
mzlendic@sfzg.hr