Abstracts Accepted for Publication

Genomics, genetic basis of disease and antigen presentation

AB0001

ASSOCIATION OF DICKKOPF1-1 POLYMORPHISMS WITH RADIOLOGICAL DAMAGE AND PERIODONTAL DISEASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that primarily affects the joints but also has extra-articular manifestations such as Periodontal Disease (PD). The Dickkopf-1 (DKK-1) may have an active role in the regulation of bone biology and patients with RA that carry genetic variants of DKK-1 have greater bone damage

Objectives: To investigate the polymorphisms of DKK-1 in patients with early RA (eRA) and its association with some rheumatic, radiological and periodontal variables.

Methods: A cross-sectional study in 63 patients with eRA according to the ACR/EULAR 2010 criteria and PD based on the AAP/CDC and Prevention criteria. Serum markers rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and anticitrullinated peptide antibodies (APCAs) were evaluated. Patients selected were over 18 and less than 65 years old and were on treatment with conventional disease modifying antirheumatic drugs. Rheumatic activity was assessed by scales disease activity score 28 and simplified disease activity index. Radiographs of hands and feet were evaluated using the Sharp-van der Heijde (SvH) and Simple Erosion Narrowing Scores (SENS). DKK-1 polymorphisms as rs1896368, rs1896367 and rs1528873 were determined using the High resolution Melting technique (Bio-Rad). A bivariate analysis was performed to determine the variables associated between polymorphism to the presence of radiological and activity scores, diagnosis and severity of PD. A regression model was performed to confirm these associations.

Results: The mean age was 48.57±11.35 years, and 76.7% were female. 11.7% had a body mass index >30 kg/m². 35% had an ESR >20 mm/h, and 56.7% had elevated CRP. RF >20 was observed in 61.7% of patients as were APCAs >20 in 43.3% of them. 30%, 42% and 1.6% of patients were homozygous for polymorphism rs1896367, rs1896368 and rs1528873 respectively. Individuals heterozygous for polymorphism rs1896367 had more frequent erosions (p=0.026) and joint space narrowing (JSN) (p=0.005) in the feet, and consequently higher SHS scores (p=0.016). These patients also had higher SENS scores (p=0.001) and more frequent erosions (p=0.02). In contrast, patients homozygous for polymorphism rs1896368 had less frequent JSN in hands and feet as assessed by SHS, as well as less presence of erosions based on the SENS scale. These findings were validated in the regression model (OR: 0.04, 95% CI:0.00–0.93;p<0.05). Finally, the presence of PD was associated with the homozygous expression of polymorphism rs1896367 (p=0.009) and the heterozygous expression of polymorphism rs1896368 (p=0.033).

Conclusions: DKK-1 polymorphisms can be associated with the presence of bone damage in patients with eRA and it could affect periodontal outcomes. While polymorphism rs1896367 seems to be associated with greater radiological compromise, polymorphism rs1896368 confers protection against bone damage in Colombian eRA patients.

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AB0002

EFFECT OF COMMON POLYMORPHISMS IN THE METHOTREXATE PHARMACOKINETIC PATHWAY ON EFFICACY/ADVERSE EFFECTS AND METHOTREXATE POLYGLUTAMATE LEVELS IN RA

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Background: Measurement of erythrocyte methotrexate polyglutamate levels (MTX-glu_n) are widely used to predict response and adverse effects to methotrexate in rheumatoid arthritis patients, but there are very few studies in which these levels were correlated with common polymorphisms in genes involved in methotrexate (MTX) pharmacokinetics. This preliminary study evaluated their utility in Asian Indian patients in a prospective study over 24 weeks.

Objectives: The objective of this study is to investigate the impact of seven common polymorphisms in genes involved in methotrexate (MTX) pharmacokinetics on response, adverse effects and methotrexate polyglutamate (MTXPG) levels in rheumatoid arthritis.

Methods: This study enrolled 117 RA patients who were treated prospectively with MTX for 24 weeks. Patients were categorised on the EULAR criteria into responders (good and moderate) and non-responders. Adverse effects were ascertained using a questionnaire. The following polymorphisms were ascertained using hydrolysis probes – rs1045642 (ABCB1 3435C>T), rs1128503 (ABCB1 1236C>T), rs10106 (FPGS 1994A>G), rs1544105 (FPGS G>A), rs11545078 (GGH 452C>T), rs3758149 (GGH –401C>T) and rs1051266 (RFC1 80G>A). RBC MTXPG1–5 levels were determined using HPLC at 4,8,16 and 24 weeks.

Results: There was a significant association of the GGH 452C>T CC genotype (OR 9.5, 95% CI 1.2 to 76.0) with response to MTX. On logistic regression, higher DAS28³ at baseline and GGH 452CC genotype were significantly associated with response (table 1); the accuracy of the model was 75%. The FPGS 1994A>G GG genotype was associated with a significantly lower risk of adverse effects to MTX (Odds Ratio 0.3 (95% CI 0.1 to 0.6)). On logistic regression, FPGS 1994GG genotype and lower BMI were significant predictors for adverse effects with an accuracy of 66%. The other polymorphisms were not associated with response or adverse effects. None of the polymorphisms were associated with change in MTXPG levels.

Conclusions: GGH 452 CC genotype was found to be associated with response to MTX and FPGS 1994 A>G GG with a lower risk of adverse effects; however, not by change in MTXPG levels.

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