
Background: Early-onset or juvenile gout (EOG) without hypoxanthine-guanine phosphoribosyltransferase enzyme deficiency (HPRT, OMIM 300323) and related to familial juvenile hyperuricemic nephropathy (UMOD, OMIM 300323) is a rare gout phenotype characterised by a first flare in adolescence or in young adulthood. While numerous genome-wide association studies (GWAS) have been done in classic late-onset gout, very few studies have been performed in EOG patients. Moreover, until now most genetic studies only assess association between pre-defined single nucleotide polymorphisms (SNP) and gout.

Objectives: Our aim was to identify the genetic variants of clinically confirmed EOG by screening all exons of gout-associated genes with targeted Next-Generation Sequencing (NGS) approach.

Methods: Twenty-six urate crystal-proven gout patients with first flare occurring before the age of 30 years were included. Gout history, comorbidities and patient characteristics were recorded. All participants provided written informed consent to genetic analysis. After DNA extraction from total blood samples, the NGS libraries were prepared with sureselect XGT (Agilent) and sequencing was performed with miseq (illumina). The multigene panel included 80 genes described in GWAS and genes involved in rare diseases such as HPRT1 and UMOD. Patients had a mean age of 37.5 ± 14.6 years, and a mean body mass index of 27.6 ± 5.7 kg/m2. Ten patients were overweight, 5 had obesity, 1 hypertension, 0 diabetes mellitus, 7 dyslipidemia and 10 chronic kidney disease stages 2–4. Mean serum urate level was 527 ± 803 μmol/L. Amongst 26 affected patients, 7 had a molecular anomaly (26.9%). Six patients harboured one rare or novel variant in ABCG2 (three Caucasian patients), ALDH16A1 (two Caucasian patients) and SLC22A11 (one African patient). Two other patients (one Caucasian and one Asian) carried an association of variants in both ABCG2 and ALDH16A1. All variants had a Minor Allele Frequency (MAF) below 0.3% or were never described in public databases. All variant were considered as probably pathogenic according to in silico predictive algorithms. Interestingly, the well-known p.Gln141Lys SNP of ABCG2 was identified in 3 Asian patients (11.5%) at homozygous level.

Conclusions: Our finding of very rare and novel pathogenic variants in ABCG2, ALDH16A1 and SLC22A11 provides better insights of the molecular pathogenesis in early-onset juvenile gout. However, our results also highlight the involvement of yet unidentified genes in this population. Disclosure of Interest: None declared


ALL-CAUSE MORTALITY AND CARDIOVASCULAR DEATH IN HYDROXYCHLOROQUINE USERS IN RHEUMATOID ARTHRITIS PATIENTS – A POPULATION BASED DANISH COHORT STUDY

K. Søeltoft1, J. Hallas2, M.C.M. Wasko3, A.B. Pedersen4, S.P. Ulrichsen4, T. Eliassen1, 1Dept of Rheumatology; 2Dept of Clinical Chemistry and Pharmacology, Odense University Hospital, Odense, Denmark; 3West Penn Hospital, Pittsburgh, USA; 4Dept of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

Background: Rheumatoid arthritis (RA) is associated with a marked increase in cardiovascular mortality and morbidity.1 The increased risk is present from the earliest stages of the disease and evidence suggests an overlap in the pathogenic features leading to RA and atherosclerosis. Hydroxychloroquine (HCQ) is used to treat RA in combination with methotrexate and has been associated with decreased risk of type II diabetes and dyslipidaemia among RA patients. Also HCQ has improved survival rates when used to treat other inflammatory diseases, e.g. systemic lupus erythematosus.2 The evidence regarding RA patients is scarce.

Objectives: We wish to examine whether HCQ would affect the incidence rates of cardiovascular diseases, type II diabetes, cardiac – and all-cause mortality among Danish RA patients in an observational cohort study.

Methods: We identified all incident RA patients during the period of 2004 through 2014 in Denmark. HCQ initiators were compared with non-users of HCQ, stratified on rheumatoid factor positivity. Each HCQ initiator was matched to a non-HCQ initiator by their propensity score (PS). In the PS all relevant available cardiovascular drugs and comorbidities were included. All together we had 3,742 RA patients in each group.

Results: We found a significant reduction in all-cause mortality and cardiovascular-related death among HCQ initiators, with a hazard ratio of 0.83 (95% confidence interval [CI] 0.71–0.97) and 0.78 (95% CI: 0.61 to 0.99), respectively. We did not find any association between HCQ use and development of type II diabetes or specific ischaemic events (myocardial infarctions and ischaemic strokes).

Disclosure of Interest: None declared