PP140—THE CONTRIBUTION OF PLATELET GLYCOPROTEINS (GPIA C807T AND GPIBA C-5T) AND CYCLOOXYGENASE 2 (COX-2 G-765C) POLYMORPHISMS TO PLATELET RESPONSE IN PATIENTS TREATED WITH ASPIRIN

S. Al-Azzam1; K.H. Alzoubi2; O. Khabour2; D. Tawalbeh1; and O. Al-Azebeh1
1Department of Clinical Pharmacy; and 2Department of Medical Laboratory Sciences, Jordan University of Science and Technology, Irbid, Jordan

Introduction: Aspirin is an antiplatelet agent commonly used in treatment of patients with high risk to develop stroke and myocardial infarction. However, interindividual variability regarding the inhibition of platelet function by aspirin is well documented. In this study, the correlation between platelet glycoproteins (GPIa C807T and GPIba C-5T) and cyclooxygenase 2 (COX-2 G-765C) polymorphisms and antiplatelet response in patients treated with aspirin was investigated.

Patients (or Materials) and Methods: Jordanian adult patients (n = 584) who are taking aspirin as an antiplatelet agent participated in the study. Platelet aggregation response was measured using Multiplate Analyzer® system. Polymerase chain reaction–restriction fragment length polymorphism assay (PCR-RFLP) was used for genotyping of the examined polymorphisms.

Results: Aspirin resistance was found in 15.8% of patients. Response to aspirin was significantly associated with GPIba C-5T polymorphism (P < 0.05). However, the GPIa C807T and COX-2 G-765C polymorphisms were not related to aspirin resistance (P > 0.05).

Conclusion: A considerable fraction of the Jordanian population is resistant to the antiplatelet effect of aspirin, which might be related to GPIba C-5T polymorphism.

Disclosure of Interest: None declared.

PP142—INFLUENCE OF THE CYP2D6 -1584C>G PROMOTER POLYMORPHISM ON THE PHENOTYPE OF DEBRISOquine IN HEALTHY VOLUNTEERS FROM CUBA AND NICARAGUA

M.E.G. Naranjo1; P. Dorado1; L.R. Calzadilla2; M. Álvarez1; R. Ramírez3; E.M. Peñas-LLedo1; B. Pérez1; I. González1,2; A. Llerena1,3; and CEIBA Consortium
1CICAB, Clinical Research Centre, Extremadura University Hospital, Badajoz, Spain; 2Hospital Psiquiátrico de La Habana; 3Faculty of Medical Sciences and Faculty of Medicine “Calisto García”, La Habana, Cuba; 4Facultad de Medicina, UNAM Universidad Autónoma Nacional de Nicaragua, León, Nicaragua; 5Hospital de Llerena, Servicio Extremño de Salud SES, L.Lerena; and 6CIBERSAM, Instituto de Salud Carlos III, Madrid, Spain

Introduction: Ultrarapid drug metabolism (UM) mediated by CYP2D6 is associated with duplicated or amplified functional CYP2D6 alleles. However, duplicated CYP2D6 alleles only explains a fraction (10%–30%) of the UM phenotype observed in Caucasian populations, and other biochemical and/or genetic factors involved in UM phenotype remain unexplained yet. CYP2D6 -1584C>G has been related with changes in CYP2D6 expression, being -1584G associated with higher expression. The aim of this study was to explore the relationship between CYP2D6 -1584C>G polymorphism and the debrisoquine hydroxylation capacity.
Patients (or Materials) and Methods: Three hundred twenty unrelated healthy individuals from Cuba and Nicaragua were included to analyze the CYP2D6 -1584C>G polymorphism using PCR-RFLP. These subjects were also previously genotyped for CYP2D6 and phenotyped for debrisoquine hydroxylation.1

Results: Individuals with -1584G allele had a lower metabolic ratio (log_{10} mean [SD]) than individuals with -1584C allele among carriers of one (-0.13 [0.33] and 0.17 [0.52], respectively; P < 0.05) or 2 (-0.32 [0.39] and -0.20 [0.44], respectively; P < 0.05) CYP2D6 active genes. No differences were observed in individuals with >2 CYP2D6 active genes (-0.85 [0.69] and -0.59 [0.40], respectively).

Conclusion: CYP2D6 -1584C>G polymorphism was related with higher debrisoquine hydroxylation capacity in individuals with 1 or 2 CYP2D6 active genes.

Financial Sources: Supported by the Institute of Health Carlos III-FIS and the European Union (FEDER) Grant P11002758, Gobierno de Extremadura, Consejería de Empleo Empresa e Innovación y Fondo Social Europeo (FSE) Grants PD10199 and BS10023, and AEXCID Cooperación Extremeña of Junta de Extremadura (11IA002). It was coordinated in the RIBEF network (Red Iberoamericana de Farmacogenética y Farmacogenómica; www.ribef.com).

Disclosure of Interest: None declared.

Reference

PP143—IMPACT OF UGT1A4 GENOTYPE IN THE CLINICAL RESPONSE TO LAMOTRIGINE IN PATIENTS WITH EPILEPSY

A. Ortega Vázquez1; P. Dorado2; S. Rojas Tomé3; I. Iris Martínez Juárez4; H. Jung Cook3; N. Monroy Jaramillo3; M.E. Alonso Vilatela3; E.M. Peñas-Lledó2; A. LLerena2; and M. Lopez Lopez1

1University Autónoma Metropolitana Unidad-Xochimilco, México, Mexico DF, Mexico; 2CICAB Clinical Research Centre, University of Extremadura Hospital and Medical School, Badajoz, Spain; and 3Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico DF, Mexico

Introduction: Epilepsy is treated with a variety of anticonvulsants including lamotrigine (LTG). Patients treated with antiepileptic drugs can exhibit large interindividual variability in clinical efficacy and adverse effects. LTG is widespread used for the treatment of partial and generalized epilepsy seizures. It is mainly metabolized by the phase II enzyme UGT1A4 (UDP-glucuronosyltransferase 1A4) to 2-N-glucuronide. Functional studies of the 2 nonsynonymous genetic polymorphisms UGT1A4*2 (P24T) and UGT1A4*3b (L48V) have shown decreased enzyme activity on various substrates, including LTG.

Aims: To investigate the impact of UGT1A4*1b, UGT1A4*2 and UGT1A4*3b polymorphism on LTG plasma levels and clinical response in epileptic patients.

Patients (or Materials) and Methods: Forty-nine patients with epilepsy (17–67 years old) treated with LTG gave informed consent to participate in the study. Nine patients were under monotherapy. Genomic DNA was extracted from peripheral blood samples by standard technique. Genotyping was performed by real-time PCR using allele-specific probes. LTG plasma levels were determined by HPLC analysis. Clinical response was evaluated by seizures control (responder, 0–1 seizure/month).

Results: The results of the present study showed a great interindividual variability in plasma levels between 1.1 and 22.3 µg/mL, even among patients under the same posology. The UGT1A4 genotype showed a tendency to modify the LTG plasma level, although no statistically difference was achieved (P = 0.1175). It was also found that .43% of the patients responded to treatment. Among mono-therapy cases, the patient with the highest LTG plasma level (9.5 µg/mL) exhibited UGT1A4 wt/*3b genotype.

Conclusion: Our results indicate that UGT1A4*1b, *2 y *3b polymorphism did not have an important impact in the clinical response to LTG in the 49 epileptic patients studied. Nevertheless, further investigations are needed with a larger sample.

Financial Sources: Supported by grant #167261 from Consejo Nacional de Ciencia y Tecnología (CONACYT), Mexico and the Institute of Health Carlos III-FIS and the European Union (FEDER) Grants P11002758, Gobierno de Extremadura, and Union Europea (Fondo Social Europeo) Grant PRIS100023 andPD10199 (MEGN), and AEXCID 11IA002, coordinated in the Iberoamerican Network of Pharmacogenetics (SIFF).

Disclosure of Interest: None declared.