P-081 - IS CHITOTORISIDASE AN USEFUL BIOMARKER FOR DIAGNOSIS AND TREATMENT MONITORING OF GAUCHER DISEASE? EXPERIENCE IN A COHORT OF 197 ARGENTINEAN PATIENTS

Drelichman Gl ¹, Soberon BC ¹, Fernández-Escobar N ¹, Ruan J ², Belinsky B ², Schenone AB ³, Detoni D ¹, Larroude M ⁴, Aguilar G ⁴, Mistry P ² et al.

1) Hospital de Ninos Ricardo Gutierrez, ciudad autonoma de Buenos Aires, Argentina. (2) Yale University School of Medicine, New Haven, CT, United States. (3) Laboratorio de Neuroquimica Dr N A Chamoles, ciudad autonoma de Buenos Aires, Argentina. (4) Centro de Diagnostico Dr Rossi, Enrique, ciudad autonoma de Buenos Aires, Argentina. Ciudad de Buenos Aires-Argentina. bsoberon@live.com

INTRODUCTION: Chitotriosidase is an established biomarker for Gaucher Disease (GD) reflecting involvement of alternatively activated macrophages in disease pathophysiology. Several limitations have been highlighted including presence of common polymorphism in CHIT1 in heterozygous form in ~30% of patients and homozygous null allele in ~6% of patients that reduces circulating levels to 50% and lack of detectable chitotriosidase, respectively. The responsible polymorphism is a 24 bp duplication in exon 10 of CHIT1 that renders the gene inactive. The high prevalence of 24bp duplication impedes the ability to compare biomarker levels among patient populations and in ~6% of individuals it is completely uninformative. OBJECTIVES: to assess the prevalence of 24 bp duplication in an entire cohort of GD patients in Argentina and concurrently measure serum chitotriosidase to further assess its biomarker properties to correlate with GD manifestations. METHODS: Serum samples (total 417) were obtained during different moments in timeline of treatment: 175 patients treated for up to 14 years with imiglucerase (ERT) and 22 patients treated with eliglustat (SRT) for up to 6 years (Table 1). Samples were analyzed for CHITO genotype and serum chitotriosidase was measured. We analyzed chitotriosidase based on presence and absence of bone disease (BD). RESULTS: CHIT1 genotyping revealed a somewhat higher proportion of CHIT1 null homozygous patients compared to other populations: 28/193, 14.50 % (vs 6.0% in other populations). Hetero carriers were also slightly over-represented:: 86/194, 44.56 % (vs 35% in other populations), with concomitant decreased prevalence of wild type homozygous allele: 79/193, 40.94 % (vs 59% in other populations). CONCLUSION: High prevalence of 24 bp polymorphism in Argentinian population therefore impedes broad application of chitotriosidase as biomarker of Gaucher disease and underscore the importance of concurrent CHIT1 genotyping to assess chitotriosidase in the clinic.