P-116 - NITISINONE DETECTION BY LCMSMS IN DRIED BLOOD SPOT AND PLASMA SAMPLES IN CHILEAN TYROSINEMIA 1 PATIENTS IN FOLLOW UP. VALIDATION SAMPLE LEVELS WITH NITISINONE DEVELOPED METHOD IN WELLCHILD LABORATORY, EVELINA CHILDREN’S HOSPITAL, LONDON.

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INTRODUCTION: Tyrosinemia type 1 (Tyr-1) is an inborn error of metabolism caused by defects in tyrosine metabolism and characterized by accumulation of tyrosine and toxic degradation products. Treatment of Tyr-1 patients is based on nitisinone (NTBC) administration. NTBC was developed as a herbicide and monitoring levels in dried blood spot (DBS) and plasma samples are necessary for optimal dosage. Sixteen patients are in active follow-up in our reference center and trimestral NTBC levels were analyzed at Evelina Children’s Hospital in London during 2016-2018. OBJECTIVE: To implement NTBC determination by LCMSMS in DBS and plasma samples and to compare NTBC levels obtained in our center with those reported by Dr. Charles Turner in London during the follow up of Tyr-1 patients between 2018-2019. METHODS: NTBC quantification by LCMSMS was implemented based on the construction of calibration curve by using mesotriene as internal standard. DBS samples were extracted using 100% methanol. ESI(+) was used as ionization method and analytes were detected by Multiple Transition Monitoring (transitions 330 > 218 for NTBC and 340 > 228 for mesotriene). Thirty DBS samples from Tyr-1 patients were analyzed in parallel with WellChild Laboratory and 26 plasma samples were analyzed for correlation with DBS levels. RESULTS: We are able to detect NTBC by LCMSMS in DBS and plasma samples from Tyr-1 patients. Our method, shows good precision, accuracy and linearity with detection limit of 0,5 nmol/L. The concentration range determined in DBS samples from Tyr-1 patients was 12,0-43,3 µmol/L and 29,7-97,6 µmol/L for plasma samples. Parallel comparison of NTBC levels in DBS samples shows values 20% higher with those analyzed in WellChild Laboratory. NTBC levels in plasma and in DBS are well correlated being 2.4 times higher in plasma. CONCLUSION: We validated in our laboratory the LCMSMS method used in the Laboratorio di Patologia Metabolica at Ospedale Bambino Gesu for the detection of NTBC in DBS and Plasma samples. NTBC determination of Chilean Tyr-1 patients in follow-up during 2018-2019 showed reproducible results, comparable with those obtained in Evelina Children’s Hospital, London. Good correlation was observed in DBS and plasma samples.