P-176 - DIAGNOSIS AND FOLLOW-UP OF PATIENTS WITH UREA CYCLE DEFECTS. REPORT OF LOCAL EXPERIENCE


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INTRODUCTION: Urea cycle disorders (UCD) are inborn errors of ammonia detoxification/arginine synthesis. The onset and severity of UCD, caused by hyperammonaemia, is highly variable; this depends on the specific mutation involved and correlates with the residual enzymatic function. The exact incidence of UCDs in Argentina is not known due to absence of newborn screening or a registry. Most of the patients are detected symptomatically, adding to high morbidity and mortality.

OBJECTIVE: To present a local experience in diagnosis, molecular findings and outcome of UCD patients from Argentina.

MATERIALS AND METHODS: Biochemical methods included determination of plasma and urinary amino acids and orotic acid through HPLC; quantification of plasma ammonia by spectrophotometry; genetic study consisted in PCR, restriction enzyme digestion assays or direct sequencing, SSCP or MLPA.

RESULTS: We present data from a single centre in Argentina, including 49 UCD cases. Most of them (26/49, 53%) presented in the neonatal period with classical presentation, and had a high mortality (25/26, 96%). Ornithine transcarbamylase (OTC) deficiency was the most common UCD, observed in 26/49 patients, with privative OTC gene mutations. Argininosuccinate synthetase (ASS) deficiency was the next most common, seen in 19 cases, most of them from a populational cluster of CTLN1 with the same mutation. Argininosuccinate lyase (ASL) deficiency was diagnosed in 4 cases presenting worldwide recurrent missense changes. We observed a poor clinical outcome after an hyperammonemic crisis with an overall all time mortality of 57% (28/49 cases), and disability in 28% (6/21) among the survivors. The average detection rate calculated in our center is 4 new UCD patients per year, 30% of what is expected per year in Argentina.

CONCLUSIONS: The majority of patients in our serie showed neonatal severe onset, with a high mortality/morbidity. The presence of a geographic cluster of high prevalence of a point mutation in ASS is highlighted. This report shows our experience in the genetic characterization of UCD and notes that these disorders are not rare but need of awareness and diagnostic tools for accurate identification, which will lead to improve outcomes through early diagnosis and timely treatment.