P-094 - TPP1 ACTIVITY IN CEREBROSPINAL FLUID OF FOUR CLN2 AFFECTED CHILDREN UNDER INTRATHECAL CERLIPONASE ALPHA THERAPY

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INTRODUCTION: Neuronal Ceroid Lipofuscinosis disease CLN2 is a neurodegenerative disorder caused by Tripeptidyl Peptidase 1 (TPP1) deficiency. It is commonly diagnosed by enzyme activity measurement in leukocyte pellet. Cerliponase alpha is a recombinant enzyme approved for use as enzyme replacement therapy (ERT). This therapy is performed at the Children’s Hospital Cordoba, Argentina, since 2017 as an intrathecal infusion into the ventricle cerebrospinal fluid (CSF) ideally every 15 days. The range of TPP1 activity in cerebral CSF remains unknown. OBJECTIVES: To develop a reference interval of TPP1 enzyme activity in CSF of controls, and to quantify the TPP1 activity in the CSF of infused subjects to follow-up the variations along the treatment. MATERIALS AND METHODS: TPP1 activity was quantified in CSF from 29 controls (lumbar puncture samples provided by Central Laboratory of the Children’s Hospital), and from 4 patients along intrathecal treatment (obtained before every infusion under informed consent of the parents). RESULTS: Control’s TPP1 activity was 19.36 - 379.50 nmol TPP1/24h/mg protein (215.24 ± 96.37 [mean ± SD] nmol TPP1/24h/mg protein). Activity of subject #1 was 0 - 638.6 nmol TPP1/24h/mg protein. Activity of subject #2 was 6.26 - 5630.69 nmol TPP1/24h/mg protein. Activity of subject #3 was 1.52 - 802.84 nmol TTP1/24h/mg protein. Activity of subject #4 was 0 - 3239.10 nmol TPP1/24h/mg protein. All individuals showed marked decrease of activity along the successive infusions, and some of the values were in the deficiency range. DISCUSSION: Spinal CSF was validated as control biological sample provider. Despite the subjects under ERT received the same doses of enzyme, activity of TPP1 in CSF showed a broad range. During the first phase of treatment, 3 out of 4 individuals showed activity near 10-fold the controls’ range. Only subject #1 showed certain stability of values along all the infusions. The remaining individuals showed a tendency to stabilization along infusions after an initial peak, with some unexpected deficient values. It remains as an open question if TPP1 activity assay could be used as a biomarker; further studies are needed for a better understanding of TPP1 activity variations along intrathecal Cerliponase therapy.