Poster # 049

REDUCED BIOTINIDASE ACTIVITY IN PATIENTS WITH CONGENITAL DISORDERS OF GLYCOSYLATION (CDG): BIOTIN AS A NEW THERAPEUTIC APPROACH?

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Background: Defects in the complex process of glycoconjugate biosynthesis underlie Congenital Disorders of Glycosylation (CDG), manifesting mostly as multi organ disease with neurodevelopmental disorder, seizures, muscular hypotonia, ataxia, cerebellar hypoplasia, heart, liver and immunological problems, coagulopathy and dysmorphism. Effective therapies are available only for a couple of the currently known >170 CDGs. Therefore, management is mainly symptomatic.

Interestingly, individuals with (partial) biotinidase deficiency (BTD; MIM #253260) can present with several of the above-mentioned symptoms of different severity that are responsive to oral biotin supplementation. Biotinidase needs glycosylation at four sides for proper functioning. It allocates biotin, which displays the prosthetic group of important carboxylases needed for gluconeogenesis, fatty acid biosynthesis and degradation of several amino acids. We hypothesize hypoglycosylation of the biotinidase in individuals with CDG contributes to their clinical presentation and might respond to oral biotin supplementation.

Methods: Dried blood spots of 6 CDG cases (3 CDG-I and 3 CDG-II, age 7–14 years) were analyzed for biotinidase activity. Oral biotin 10 mg/day was given during one year. Adaptive Behavior Assessment System II (ABAS-II) questionnaires were completed by parents/caretakers before the start of treatment, after 6 and 12 months.

Results: Medium enzyme activity in 6 individuals with CDG was 47% (range 12–80%; reference range 20–200%). ABAS-II questionnaires indicated improved skills concerning communication (5/6 individuals), community use (4/6), functional pre-academics (5/6), home and living (5/6), health and safety (6/6), leisure (5/6), self-care (5/6), self-direction (5/6) and social (5/6).

Conclusions: We hypothesized a (partial) BTD and indeed measured a medium biotinidase activity just above the range of partial biotinidase deficiency (10–30%) in a pilot study of six individuals with CDG.

Notably, the clinical severity of BTD is not linearly correlated to the residual enzyme activity and biotin has no known side effects. During biotin supplementation of six individuals with CDG their parents/caretakers reported improved psychomotor abilities.

Obviously, our study has several limitation (e.g. small number of included individuals, observers not blinded) but still it encouraged us to further evaluate possible BTD and biotin supplementation in an ongoing study with 80 individuals with CDG.

Biotin supplementation may represent a simple, safe and inexpensive add on-management option which is not restricted to a specific CDG type.

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