GENETIC DISORDERS

Quality Of Life in Individuals with CDKL5 Deficiency Disorder

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Investigators from The University of Western Australia in Perth and Children's Hospital Colorado University studied the quality of life (QOL) in children with CDKL5 Deficiency Disorder (CDD). The results indicated that lower functional abilities were associated with poorer quality of life. [1]

COMMENTARY. CDD is a rare developmental epileptic encephalopathy caused by mutations in the cyclin-dependent kinase-like 5 (CDKL5) gene. It is now considered a developmental and epileptic encephalopathy [1] with seizures early in life (e.g. infantile spasms, myoclonic seizures and tonic-clonic seizures) and inability to walk or talk. Other features include sleep difficulties, constipation and cortical visual impairment. Seizure control is challenging and often multiple anticonvulsants are needed. Vagal nerve stimulation and the ketogenic diet have shown variable improvement in some cases [2].

Progress in clinical understanding, especially regarding the spectrum of functional ability, seizure patterns, and other comorbidities, was initially slow but accelerated in 2012 with the establishment of the ICDD [1]. The first output from the database examined developmental milestones in 127 children with CDD, where the milestones were significantly delayed and worse for males than females [3].

A pilot study was conducted on 25 patients with CDKL5 identifying the QOL domains, where semi-structured telephone interviews were used to explore areas that affected QOL. Patients were divided into three age groups: 3-5, 6-18, and older than 18. This was the first study to conceptualize factors important for individuals with CDD [4]. However, a novel validated QOL scale, and quantitative assessment was administered for the first time in Leonard H et.al study where QOL for patients was evaluated using QI Disability which was an instrument specifically developed to measure total and specific domains of QOL, including physical health, positive emotions, negative emotions, social interaction, leisure and the outdoors (leisure) and independence [1]. The severity of the functional impairment adversely impacted QOL. This correlated study factors like family QOL, severe sleep difficulties, child behavior, and increased hospitalization. Patients using only one anti-epileptic medication had a better quality of life than those using three or more [1]. This demonstrates that several factors can affect QOL, especially with reports now expanding the phenotype of the CDKL5 to include patients without seizures but with apparent behavioral symptomatology [5].

Comprehensive care and support have essential roles to play in helping these families. Also, disparity of QOL was identified and was highest in North America and lowest in Australia and "other" countries, which might be due to an ascertainment bias selecting more socioeconomically advantaged families in the study [1]. More research in this area will help to develop a systematic approach to treating CDD patients, understand the role of environmental support in improving QOL and to identify and address factors contributing to healthcare disparities. The International Foundation for CDKL5 Research and the ICDD can provide excellent resources to achieve these goals.

Disclosures

The author has declared that no competing interests exist.

References

1. Leonard H, Junaid M, Wong K, Demarest S, Downs J. Exploring quality of life in individuals with a severe developmental and epileptic encephalopathy, CDKL5 Deficiency Disorder. Epilepsy Res. 2021 Jan;169:106521. https://doi.org/10.1016/j.eplepsyres.2020.106521; Epub ahead of print. PMID:33341033
2. Lim Z, Wong K, Olson HE, Bergin AM, Downs J, Leonard H. Use of the ketogenic diet to manage refractory epilepsy in CDKL5 disorder: experience of >100 patients. Epilepsia. 2017 Aug;58(8):1415–22. https://doi.org/10.1111/epi.13813 PMID:28605011
3. Fehr S, Leonard H, Ho G, Williams S, de Klerk N, Forbes D, et al. There is variability in the attainment of developmental milestones in the CDKL5 disorder. J Neurodev Disord. 2015;7(1):2. https://doi.org/10.1186/1866-1955-7-2 PMID:25657822
4. Tangarorang J, Leonard H, Epstein A, Downs J. A framework for understanding quality of life domains in individuals with the CDKL5 deficiency disorder. Am J Med Genet A. 2019 Feb;179(2):249–56. https://doi.org/10.1002/ajmg.a.61012 PMID:30561084
5. MacKay CI, Bick D, Prokop JW, Muñoz I, Rouse J, Downs J, et al. Expanding the phenotype of the CDKL5 deficiency disorder: are seizures mandatory? Am J Med Genet A. 2020 May;182(5):1217–22. https://doi.org/10.1002/ajmg.a.61504 PMID:32034940

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