Photopic electroretinogram (ERG) and colour vision (CV) evaluation in a presumptive sporadic Duchenne muscular dystrophy (DMD) cohort in northern India

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Purpose

DMD is an X-linked recessive disorder [mutations in the *dystrophin* gene on chromosome Xp21.2] affecting about 1/5000 male live births. *Dystrophin* maintains muscle strength and participates in central nervous system [CNS] and retinal signaling. Deletion upstream to position 45 in the DMD gene results in more deleterious frameshift mutations than those downstream, which have a good amount of residual dystrophin left. A great deal of genetic and clinical heterogeneity exists in presentation. Presumptive sporadic DMD on pedigree charting is observed in about 33% cases and may be due to *de novo* mutations as well as maternal transmission. This cross-sectional study aimed to evaluate CV and photopic ERG as functional evidence of retinal malfunctioning in a cohort of children with presumptive sporadic [on 3 generation pedigree charting] DMD [genetic or muscle biopsy diagnosis] in a tertiary care pediatric ophthalmology centre in northern India.

Methods

Complete ophthalmic evaluation of 19 male children [8±1.8years] with DMD, 13

diagnosed on genetic analysis and 6 on muscle biopsy, was performed. Detailed CV assessment was done with Ishihara, Hardy-Rand-Rittler {HRR}, Farnsworth and Lanthony saturated and desaturated tests and photopic ERG was performed on Metrovision MonPack One ERG module, France, 2011. The mothers were evaluated as controls.

Results

Anterior and posterior segment ocular evaluation was normal with best corrected visual acuity [BCVA] of logMAR 0.00 in both eyes in all cases. Red-green CV deficit was present in 3 cases with all demonstrating a/b wave inversion and attenuation of b waves on photopic ERG. They had deletions in exon 17-21, 45-90 and 60 respectively. In 10 subjects with normal CV, only 1 subject with deletion in exon 46-47 had normal photopic ERG waves. In 6 subjects with biopsy proven DMD, 1 had normal photopic ERG waves while the rest showed b wave attenuation. The mothers of these children did not demonstrate any functional or structural ocular anomalies.

Conclusions

This study, unique in the north Indian cohort, demonstrates significant attenuation of photopic ERG waves in 17/19 and red-green CV deficit in 3/19 presumptive sporadic cases of DMD irrespective of the position of exon deletion. These tests were however not useful in identifying the carrier status of the mothers, as these functions were normal in them.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.

DMD is a life-limiting X-linked recessive and sometimes sporadic disorder causing progressive muscle weakness and leading to death by late second decade. DMD results from mutations, usually exon deletions in the *dystrophin* (*DMD*) gene [79 exons] on chromosome Xp21.2. Dystrophin connects cytoskeleton to extracellular matrix in the muscle thus increasing its strength when mechanically stretched and also has signaling roles in the brain and retina. Thus, skeletal muscles, brain and eye are the major organs affected in DMD, where abnormal or no dystrophin is produced. While the muscle and brain impairments are obvious, the ocular presentations are more subtle and often ignored because it does not significantly affect visual acuity and the focus is on more life-threatening manifestations of the disease. Photopic ERG and colour vision, both parameters for assessing cone functions [which specifically have dystrophin in the signaling pathway] were hypothesized to have a correlation with the region of exon deletion as has been observed with neurodevelopmental

impairments associated with DMD. This correlation was thought to be relevant based on the assumption that distal mutations manifest with much milder symptoms as may be observed in Beckers muscular dystrophy [BMD] and may thus aid prognosticate the course of the disease.