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Corneal nerve and nerve conduction abnormalities in children with type 1 diabetes

Aim: This study aimed to compare corneal confocal microscopy (CCM) with neuropathic symptoms, signs, and objective measures of neuropathy for the diagnosis of diabetic neuropathy in children with type 1 diabetes (T1DM).
Methods: Eighty-three children with T1DM (mean age 14.8 years, range 8.4–18.3 years, mean duration 8.9 years) and 83 age-matched healthy controls underwent the assessment of neuropathy symptoms, signs, nerve conduction studies (NCS), quantitative sensory (QST) and autonomic function testing (AFT) and CCM.
Results: Only 4% of children with T1DM had subclinical neuropathy. There was a significant reduction in corneal nerve fibre density (P=0.001), branch density (P=0.006) and length (P=0.002) in children with T1DM compared to healthy controls. Furthermore, children with T1DM had significantly lower sural sensory and tibial motor nerve amplitude and conduction velocity (all P<0.004). However, no significant differences were found in vibration, cooling and warm perception thresholds and deep breathing heart rate variability in children with T1DM compared to healthy controls. Body mass index negatively correlated with corneal branch density and length.
Conclusions: There is a reduction in corneal nerve parameters in children with T1DM. CCM may allow rapid subclinical neuropathy assessment in children and adolescents with T1DM.

Comments. While diabetic neuropathy is not common in children and adolescents, subclinical neuropathy has been observed in about half of all children with T1DM with a duration of ≥5 years and up to 25% of children with newly diagnosed T1DM (Mah JK and Pacaud D *Handb Clin Neurol. 2014;126:123-43*). The screening tests for diabetic neuropathy in adults might be unreliable in pediatric patients which makes the diagnosis of early diabetic neuropathy even more challenging. CCM is an established objective technique for the assessment of small nerve fibre damage.
The current study is the most comprehensive study to date comparing CCM measures against standard neuropathy measures in children. Children with T1DM had a significant reduction in CCM parameters and abnormal NCS compared to healthy controls. Furthermore, while in adults several risk factors for corneal nerve loss have been identified, no such associations were seen in the current study except for BMI. As the authors explained, these differences can be attributed to the metabolic control, lifestyle, genetic background, relatively short diabetes duration, age, and relatively normal lipid levels. There were no significant differences in QST and ATF between children with T1DM and healthy controls. This is in contrast with previously reported results in systematic reviews (Kallinikou D et al *Diabetes Metab Res Rev. 2019;e3178*; Franceschi R et al *Acta Diabetol. 2022;59:293-308*) where different populations were studied, various methods for QST and ATF used and not homogeneous diagnostic criteria applied.
Indeed, only 4% of children had subclinical neuropathy, which made it impossible to statistically compare the measurements of CCM. Nevertheless, CCM parameters were shown to be lower in the subclinical neuropathy group. This study confirms that CCM may be utilised for the assessment of subclinical diabetic neuropathy, however, longitudinal studies are needed to assess the predictive value of CCM for the development of clinical neuropathy.

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Reference. Pacaud D, Romanchuk KG, Virtanen H, Ferdousi M, Nettel-Aguirre A, Mah JK, Tavakoli M, Zochodne DW, Malik RA. Corneal nerve and nerve conduction abnormalities in children with type 1 diabetes. Pediatr Diabetes. 2022 Sep 21. doi: 10.1111/pedi.13419. Epub ahead of print. PMID: 36131228.
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