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CLINICAL INVESTIGATIONS

Lanthony 15-Hue Desaturated Test for Screening of Early Color Vision Defects in Uncomplicated Juvenile Diabetes

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Purpose: To identify the most appropriate test for screening of early color vision abnormalities in uncomplicated juvenile diabetes.

Methods: Enrolled in this study were 39 diabetic adolescents, characterized by optimal Early Treatment Diabetic Retinopathy Study criteria for visual acuity, transparent dioptric means and angiographically normal retinas. Color vision was examined with Standard Pseudoisochromatic Plates (Part 2, SPP2), Roth 28-Hue Test (R28), Farnsworth-Munsell 100-Hue Tests (FM100), and Lanthony 15-Hue Desaturated Test (L15). Color confusion score (CCS) and desaturation angle (DSAT) were measured on L15 only. Thirty-nine normal subjects served as a control group. Poor metabolic control was an exclusion criteria.

Results: CCS was significantly higher in the patients than in the controls (37.8 ± 11.1 vs $0 \pm$ $P < .001$) and normal scores were found in only 4 diabetic patients. DSAT values were spread, not showing a well-defined axis of the defect. The results of FM100 were clinically reliable but affected by a longer execution time. R28 and SPP2 demonstrated a low sensitivity, as all patients scored normally with both tests.

Conclusions: Impaired color vision is a common observation even in patients with uncomplicated juvenile diabetes. Our results indicate that L15 is the most suitable test for screening of early color vision abnormalities in these subjects. **Jpn J Ophthalmol 2001;45:607–611** © 2001 Japanese Ophthalmological Society

Key Words: Adolescence, color vision, diabetic retinopathy, juvenile diabetes, Lanthony 15-Hue Desaturated Test.

Introduction

Early diagnosis of diabetic retinopathy (DR), by far the most frequent complication of diabetes,[1] can slow its progression and help to prevent blindness.[2,3]

Impaired hue discrimination is a common observation among participants enrolled in the Early Treatment Diabetic Retinopathy Study (ETDRS)[4]: in particular, a tritan-like defect is usually prominent and increases in magnitude with increasing severity of macular edema. Therefore, color vision measurements have also been suggested for early detection of changes in visual function in diabetic patients.[5]

Although hue discrimination in diabetic subjects without retinopathy or with only microaneurysms has been reported to not differ significantly from controls,[6] other studies disagree, concluding, on the contrary, that diabetic patients show abnormal results in color vision tests[7,8] and a tritanopic reduction in chromatic-contrast threshold[9] when compared with normal controls. However, color vision testing could not distinguish between type 1 diabetic patients with and without retinopathy.[7] Recently, even though it cannot be considered a test for chromatic discrimination, blue-on-yellow perimetry has been suggested as a useful and sensitive tool for detection of preclinical visual field defects in diabetic children with microalbuminuria but without clinically detectable retinopathy.[10,11]

In light of all these findings, the aim of the present study was to determine, in a well-characterized group of uncomplicated juvenile diabetic patients, whether or not significant color vision abnormalities

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existed even in the absence of DR and, in this case, which test was most suitable for clinical screening, combining accuracy and sensitivity with a short execution time.

Materials and Methods

Thirty-nine carefully selected postpubertal diabetic adolescents (15 male and 24 female; mean age = 17.14 ± 8.2 years), regularly attending the Center for the Study of Diabetes (Institute of Internal Medicine II, University of Rome "La Sapienza") and classified according to the National Diabetes Data Group criteria,[12] were enrolled. Selection was made by the same diabetologist on the basis of the following inclusion criteria: type 1 insulin-dependent diabetes mellitus, as evidenced by deficient C-peptide secretion; duration of the disease longer than 5 years; good metabolic control lasting more than 3 months ($HbA_{1c} < 7\%$). Thirty-nine healthy normal subjects, age- and sex-matched, served as a control group.

Exclusion criteria were poor metabolic control ($HbA_{1c} > 7\%$), "borderline" hypertension (>140/90 mm Hg), DR, smoking habit, pregnancy, cataract, aphakia or pseudophakia, intraocular pressure > 21 mm Hg, refractive error > ± 4 D, or other systemic diseases.

For all patients we recorded: sex, age at examination, age at diagnosis of diabetes, duration of diabetes, metabolic control, therapy, blood pressure. None of our subjects was taking medication other than subcutaneous human insulin (regular and long-acting).

Glycosylated haemoglobin (HbA_{1c}) was determined spectrophotometrically using reagents from Bio-Rad (Richmond, CA, USA) on 3 mL of blood drawn into evacuated siliconized tubes containing EDTA. The nondiabetic range used was 4.0–6.0%. In order to determine serum glucose and other metabolic parameters, blood was drawn into evacuated siliconized tubes and measurements were made by an autoanalyzer (Boehringer Mannheim, FRG) using enzymatic methods.

The absence of microalbuminuria (30–300 mg day^{-1}: Albustix-Ames, Miles, Elkhart, IN, USA) was confirmed in at least three samples of early morning urine collected in a 6-month period in the absence of infections or other renal diseases.[13] Blood pressure and serum creatinine concentrations were determined in order to evaluate renal function.

All necessary ethical approvals were obtained from the University Ethics Committee, and the study itself was conducted in compliance with the Declaration of Helsinki. All subjects were fully informed about the nature of the study and, thereafter, gave their written consent.

All patients underwent a careful ophthalmological examination that included best corrected ETDRS visual acuity, applanation tonometry, and retinal biomicroscopy using high positive power precorneal lenses (Super Field and +78D Volk Lenses). Retinography and fluorescein angiography (Heidelberg Retina Angiograph, FRG) were performed in order to ensure that only subjects with angiographically normal retinas were included in this study. Hue discrimination was examined by four different tests: (a) a more rapid test: The Ichikawa-Hukami-Tanabe-Kawakami Standard Pseudoisochromatic Plates for acquired color vision defects (Part 2, SPP2). These are 10 test plates (the first 2 are intended for demonstration only) in which a matrix of dots are arranged to form a number in the center. The dots making up the numbers are visible to people with normal color vision but are confused with adjacent colors by those who are blue/yellow or red/green deficient. (b) three more accurate tests, in which a series of colored tiles—28 in the Roth 28-Hue Tests (R28), 84 in the Farnsworth-Munsell 100-Hue Tests (FM100) and 15 in the Lanthony 15-Hue Desaturated Test (L15)—are arranged in separate trays. The trays of tiles are taken one at a time and jumbled; thereafter, the patient is asked to rearrange the tiles in chromatic order. The misalignment of the tiles from their correct position is then scored and marked on a standard chart, and the greater the displacement the higher the score. On L15 only, whose color tiles are characterized by a lower saturation and a higher brightness, color confusion score (CCS) and desaturation angle (DSAT) were measured using an Apple-Macintosh program (software by K. Huie, University of California—Berkeley, Berkeley, CA, USA). According to the regulations of the Commission Internationale de l'Éclairage (CIE), which recommends a standard D_{65} illumination for color vision testing (color temperature of 6504 K, close to daylight), all tests were performed at a 50 cm distance from the eye, using a 100-Watt white xenon lamp at a 1000-Lux luminance.

Data are expressed as means ± SD, unless otherwise indicated. Comparisons between cases and controls were performed using the two-tailed paired and unpaired Student *t*-test, whenever appropriate; Mann-Whitney *U*-test was applied in the case of variables with a nonparametric distribution, such as circulating HbA_{1c}. A P value of less than .05 was considered significant.

Table 1. Clinical and Biochemical Findings of Insulin-dependent Patients and Healthy Controls*

Patients	Cases (N = 39)	Controls (N = 39)	*P* Value †
Age (years)	17.14 ± 8.2	18.1 ± 3.1	NS
Sex (M/F)	15/24	17/22	–
Age at diagnosis of diabetes (years)	11.3 ± 2.7	–	
Duration of diabetes (years)	6.2 ± 1.1	–	
Systolic blood pressure (mm Hg)	122.7 ± 9.4	120.0 ± 5.5	NS
Diastolic blood pressure (mm Hg)	74.1 ± 9.1	72.5 ± 6.7	NS
Glycosylated haemoglobin (%)	6.2 ± 0.2	4.5 ± 0.6	<.001
Insulin therapy	Yes	–	
Microalbuminuria	Absent	–	
Creatinine (mmol/L)	74.48 ± 13.26	70.80 ± 11.30	NS
ETDRS visual acuity [LogMAR]	1.08 ± 0.15 [0.03]	1.07 ± 0.24 [0.03]	NS
Diabetic retinopathy	Absent	–	

* n: mean ± SD.
† NS: not significant.

Results

Table 1 summarizes both the clinical features and the laboratory findings of the diabetic cases and the healthy controls. No statistically significant differences in age, sex, blood pressure, renal function, and ETDRS visual acuity were found between the two groups of subjects. All subjects (cases and controls) had transparent dioptric means and angiographically normal retinas. Microalbuminuria was not detected in the diabetic cases.

Color Vision Tests

Color vision tests are shown in Table 2. While in R28 and SPP2 results there was no distinction between diabetic cases and normal controls, FM100 and L15, on the contrary, yielded clinically reliable distinguishing results, as only three (7.7%) and four (10.25%) diabetic cases, respectively, scored normally in these tests ($P < .001$). However, a longer execution time was necessary for completing FM100, compared to L15 (8.4 ± 3.1 vs 1.5 ± 2.2 minutes; $P < .001$). Mean CCS, measured on L15 only, are reported in Table 2, while Figure 1 shows an example of a normal and a diabetic L15-plot with calculated CCS and DSAT.

Discussion

Impaired color discrimination is a common observation even in diabetic patients with microalbuminuria but without clinically detectable DR[1011], and a selective reduction of the short wavelength-sensitive cone electroretinogram has been reported already.[14] Increased retinal blood flow, mild intraretinal edema, reduced retinal oxygenation, and accelerated

Table 2. Color Vision Test Scores in Insulin-Dependent Patients and in Healthy Controls*

Patients	Cases (N = 39)	Controls (N = 39)	*P* Value †
Standard Pseudoisochromatic Plates (Part 2)			
Normal	39 (100)	39 (100)	NS
Abnormal	–	–	–
Roth 28-Hue Test			
Normal	39 (100)	39 (100)	NS
Abnormal	–	–	–
Farnsworth-Munsell 100-Hue Test			
Normal	3 (7.7)	39 (100)	<.001
Abnormal	36 (92.3)	–	<.001
Lanthony 15-Hue Desaturated Test			
Normal	4 (10.25)	39 (100)	<.001
Abnormal	35 (89.75)	–	<.001
Colour confusion score	37.8 ± 11.1	0 ± 0	<.001
Desaturation angle	Not defined	–	–

* n: mean ± SD. Values in parentheses are percentages.
† NS: not significant.

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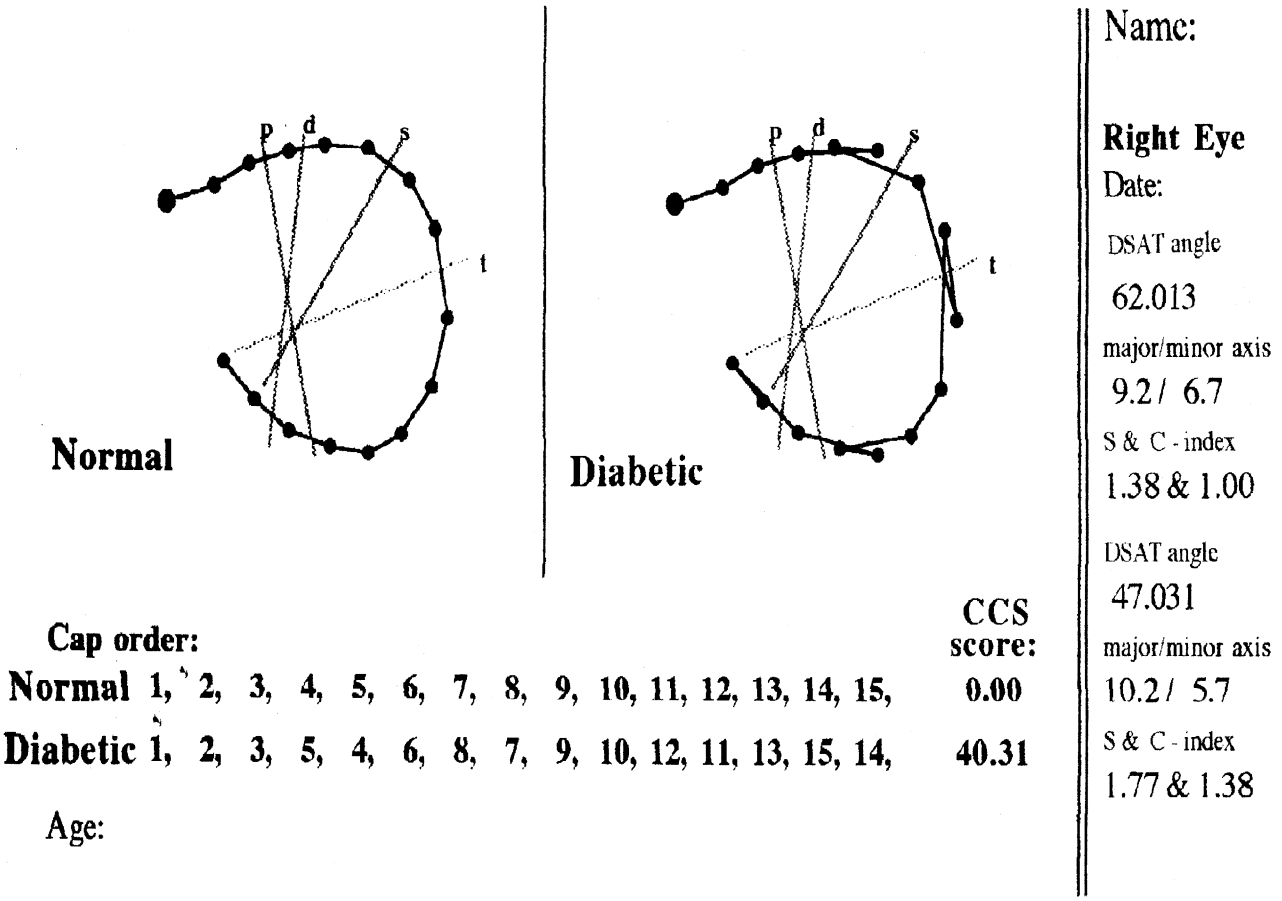

Figure 1. Example of Lanthony 15-Hue Desaturated Test scores in insulin-dependent diabetes mellitus patients and in normal controls. CCS: color confusion score, DSAT angle: desaturation angle, axis of chromatic defect: p: protan, d: deutan, s: scotopic, t: tritan. (Apple-Macintosh software by K. Huie, University of California—Berkeley, Berkeley, CA, USA).

yellowing of the lens have been related to the abnormal color perception in adult phakic type 1 subjects,[9,15–17] whereas some evidence exists for a correlation between changes in chromatic discrimination and poor glycemic control in children with diabetes of short duration.[18] However, prospective studies are required to assess this relationship over a long time period.

As color vision tests do not alter the current treatment guidelines and have no potential impact on patient care, their use is actually not yet recommended in routine eye examinations. Nevertheless, the presence of chromatic abnormalities, even in diabetic patients without DR, might serve as marker of vulnerability, helping to identify a subgroup of patients at a higher risk for complications.

The possibility of applying a color vision test (eg, SPP2, L15 and/or FM100) as an early risk indicator in the clinical monitoring of a disease has been already evaluated in several different fields: vigabatrin or carbamazepine monotherapy for epilepsy[19]; chloroquine retinopathy[20]; ethambutol treatment for tuberculosis[21]; occupational exposure to metallic mercury[22]; keratoconjunctivitis sicca[23]; diabetic macular edema.[24]

Our study was designed to determine the most appropriate test for screening of early color vision abnormalities in uncomplicated juvenile diabetic patients. In order to avoid metabolic interference with our data, all diabetic subjects were required to have good metabolic control ($HbA_{1c} < 7\%$). The presence of DR (even only a few microaneurysms), microalbuminuria, and/or any type of lens changes identified by slit-lamp examination, were exclusion criteria (Table 1).

Statistically significant results were found using FM100 and L15, as only very few diabetic patients scored normally (Table 2). The results of both tests

were considered clinically reliable even though FM100 was affected by a longer execution time. Most useful was the CCS calculation, which enabled us to numerically evaluate even minimal errors in the cap order (Figure 1). On the contrary, SPP2 and R28 showed too low a sensitivity to be of any clinical utility, as normal scores were attained by all cases with both tests (Table 2).

The origin of such a mild color vision abnormality as reported in this paper is uncertain. Some hypothetical causes of abnormal chromatic discrimination, as listed above, excluded patients from this study: in fact, all included patients had transparent dioptric means, optimal glycemic control and angiographically normal retinas. Moreover, one might speculate if this early hue abnormality might predict the future onset of a prominent tritan-like defect, as reported in the ETDRS study,[4] as well as retinopathy, cataract or neuropathy. Further investigations on larger diabetic populations and a long follow-up are necessary in order to clarify this issue.

However, although not conclusive, these preliminary results seem to suggest that L15 might be the most suitable test for screening of early color vision defects in uncomplicated juvenile diabetes patients, because L15 combines accuracy and sensitivity with a short execution time.

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References

1. Moss SE, Klein R, Klein BEK. The 14-year incidence of visual loss in a diabetic population. Ophthalmology 1998;105:998–1003.
2. Gandorfer A, Ulbig M. Diabetic retinopathy screening is a requirement. Don't wait until vision becomes impaired. MMW Fortschr Med 2000;142:26–9.
3. Danne T, Kordonouri O, Enders I, Hovener G. Monitoring for retinopathy in children and adolescents with type 1 diabetes. Acta Paediatr 1998;425(Suppl):35–41.
4. Fong DS, Barton FB, Bresnick GH. Impaired color vision associated with diabetic retinopathy: Early Treatment Diabetic Retinopathy Study Report No. 15. Am J Ophthalmol 1999; 128:612–17.
5. Ismail GM, Whitaker D. Early detection of changes in visual function in diabetes mellitus. Ophthalmic Physiol Opt 1998; 18:3–12.
6. Fristrom B. Peripheral and central colour contrast sensitivity in diabetes. Acta Ophthalmol Scand 1998;76:541–5.
7. North RV, Farrell U, Banford D, et al. Visual function in young IDDM patients over 8 years of age. A 4-year longitudinal study. Diabetes Care 1997;20:1724–30.
8. Malagola R, Gargiulo P, Giusti C, et al. Screening of early colour vision defects in insulin dependent diabetic patients with background retinopathy. ARVO abstract. Invest Ophthalmol Vis Sci 1994;35:1593. Abstract No. 1571.
9. Tregear SJ, Knowles PJ, Ripley LG, Casswell AG. Chromatic-contrast threshold impairment in diabetes. Eye 1997; 11:537–46.
10. Lobefalo L, Verrotti A, Mastropasqua L, et al. Colour and achromatic perimetry in diabetic children without retinopathy. Diabetologia 1998;41:247–8.
11. Lobefalo L, Verrotti A, Mastropasqua L, et al. Blue-on-yellow and achromatic perimetry in diabetic children without retinopathy. Diabetes Care 1998;21:2003–6.
12. National Diabetes Data Group. Classification of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979;28:1039–57.
13. Mogensen CE, Schmitz O. The diabetic kidney: from hyperfiltration and microalbuminuria to end-stage renal failure. Med Clin North Am 1988;72:1465.
14. Yamamoto S, Takeuchi S, Kamiyama M. The short wavelength-sensitive cone electroretinogram in diabetes: relationship to systemic factors. Doc Ophthalmol 1997–98;94:193–200.
15. Findl O, Dallinger S, Rami B, et al. Ocular haemodynamics and colour contrast sensitivity in patients with type 1 diabetes. Br J Ophthalmol 2000;84:493–8.
16. Kessel L, Alsing A, Larsen M. Diabetic versus non-diabetic colour vision after cataract surgery. Br J Ophthalmol 1999; 83:1042–5.
17. Dean FM, Arden GB, Dornhorst A. Partial reversal of protan and tritan colour defects with inhaled oxygen in insulin dependent diabetic subjects. Br J Ophthalmol 1997;81:27–30.
18. Ewing FM, Deary IJ, Strachan MW, Frier BM. Seeing beyond retinopathy in diabetes: electrophysiological and psychophysical abnormalities and alterations in vision. Endocr Rev 1998;19:462–76.
19. Nousiainen I, Kalvainen R, Mantyjarvi M. Colour vision in epilepsy patients treated with vigabatrin or carbamazepine monotherapy. Ophthalmology 2000;107:884–8.
20. Vu BL, Easterbrook M, Hovis JK. Detection of colour vision defects in chloroquine retinopathy. Ophthalmology 1999; 106:1799–803.
21. Sjoerdsma T, Kamermans M, Spekreijse H. Effect of the tuberculostaticum ethambutol and stimulus intensity on chromatic discrimination in man. Vision Res 1999;39:2955–62.
22. Cavalleri A, Gobba F. Reversible colour vision loss in occupational exposure to metallic mercury. Environ Res 1998; 77:173–7.
23. Rieger G. Colour discrimination in patients with keratoconjunctivitis sicca before and after artificial tear application. Wien Klin Wochenschr 1998;110:296–7.
24. Maàr N, Tittl M, Stur M, Zajic B, Reitner A. A new colour vision arrangement test to detect functional changes in diabetic macular edema. Br J Ophthalmol 2001;85:47–51.