Blue-On-Yellow and Achromatic Perimetry in Diabetic Children Without Retinopathy

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OBJECTIVE — We compared blue-on-yellow perimetry with achromatic perimetry to determine whether the first was more sensitive in detecting visual field defects.

RESEARCH DESIGN AND METHODS — We studied 50 children and adolescents (22 male, 28 female) with IDDM, ranging in age from 10.1 to 16.3 years (mean 13.3 ± 2.1 years), with a disease duration of 5.2–10.0 years (mean 7.1 ± 1.9 years). Patients were divided into subgroups according to the presence of persistent microalbuminuria. No one had signs of diabetic retinopathy when studied with fluorescein angiography.

RESULTS — By achromatic perimetry, the analysis of subareas of the central 30° of the visual field (0–9°; 10–18°; out of 18°) showed no differences between diabetic subgroups in the central 18° of the visual field, while a significant difference between the same subgroups was found outside the 18° of the 24-2 program of the Humphrey perimeter ($P = 0.027$). By blue-on-yellow perimetry, in all three of the perimetric subareas evaluated, the sensitivity was lower in microalbuminuric patients than in normoalbuminuric ones. The differential sensitivity between the perimetric tests performed with blue-on-yellow and with achromatic stimuli showed statistically significant data, with a higher level of significance in the central 18° ($P < 0.0001$) than outside the 18° ($P = 0.033$).

CONCLUSIONS — Our study suggests that blue-on-yellow perimetry is more useful and more sensitive than achromatic perimetry in the detection of preclinical visual field defects in diabetic children with microalbuminuria but without clinically detectable retinopathy.

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In the last few years, many authors (1–4) have demonstrated that diabetic patients without fluorescein angiographic signs of retinopathy can have initial psychophysical abnormalities, particularly if they have diabetic nephropathy (5). In fact, a link between retinopathy and nephropathy has been reported (6–9). In a previous study, we showed an inverse relationship between microalbuminuria and retinal sensitivity tested with achromatic perimetry (white-on-white stimuli) in diabetic children without retinopathy (5).

Recently, increasing interest has been given to the use of color perimetry (10–12), and some authors have demonstrated that blue-on-yellow perimetry is more sensitive than achromatic perimetry in demonstrating subtle visual defects not evidenced by using achromatic perimetry (11,13–18). For this reason, we decided to evaluate blue-on-yellow perimetry and compare the results with achromatic perimetry and to establish whether color perimetry can be useful for detecting functional impairment in a diabetic population at risk of developing retinopathy, i.e., having microalbuminuria.

RESEARCH DESIGN AND METHODS

We studied 50 children and adolescents (22 males, 28 females) with IDDM, ranging in age from 10.1 to 16.3 years (mean 13.3 ± 2.1 years), with a disease duration of 5.2–10.0 years (mean 7.1 ± 1.9 years), and with HbA_{1c} values of 6.0– 8.4%.

All patients selected for the study had the following characteristics:

- Glycemic control evaluated by HbA_{1c} <9%
- Glycemic values of 89–125 mg/dl before the functional examination
- Corrected visual acuity >0.8
- Refractive errors (if present) less than ± 1 spherical and ± 1 cylindrical diopters and fully corrected during examination
- Clear optic media (determined using the IntraOptics opacity lens meter)
- No fluorescein angiographic signs of retinopathy
- Absence of diabetic peripheral and autonomic neuropathy

Fifty normal age- and sex-matched subjects served as a control group; they were children attending the pediatric department for growth problems without endocrinological/ophthalmological diseases (e.g., short-normal stature).

All patients underwent the following monocular examinations, testing the right eye first (100 eyes): *1*) chromatic sense (Farnsworth 100 HUE), with the evaluation of total error score (TES); *2*) two threshold visual fields, to reduce learning effect, not evaluated in the study; and *3*) central static automated perimetry (in all patients, pupil size was >3 mm), performed with both achromatic and blue-on-yellow stimuli.

Patients were divided into subgroups according to the presence of persistent microalbuminuria, which was defined as an albumin excretion rate (AER) >20 μg/min in at least six urine examinations carried out every 2 months in the last year before the beginning of the study. Group A included microalbuminuric patients, 10

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Abbreviations: AER, albumin excretion rate; ANOVA, analysis of variance; TES, total error score.

A table elsewhere in this issue shows conventional and Sytème International (SI) units and conversion factors for many substances.

Table 1—*Foveal threshold and mean sensitivity in the central 30° tested with achromatic and with blue-on-yellow perimetry in diabetic subgroups and control subjects*

	Foveal threshold (db)		Mean sensitivity (db)	
	Achromatic	Blue-on-yellow	Achromatic	Blue-on-yellow
Microalbuminuric (group A)	32.75 ± 1.51	21.18 ± 1.55	29.14 ± 1.99	17.14 ± 1.42*†
Normoalbuminuric (group B)	32.89 ± 1.72	21.57 ± 1.49	29.95 ± 2.09	19.55 ± 1.84
Control	33.04 ± 1.93	21.69 ± 1.37	30.27 ± 4.15	19.70 ± 1.65

Data are means ± SD. db, decibels. *$P < 0.00001$ vs. normoalbuminuric patients; †$P < 0.00001$ vs. control subjects.

males and 12 females, and group B included normoalbuminuric patients, 12 males and 16 females. The mean AER in group A was 35.19 ± 13.93 μg · min^{-1} · 1.73 mq^{-1} (range 22.1–78.2), and in group B it was 9.0 ± 4.77 μg · min^{-1} · 1.73 mq^{-1} (range 3.2–19.1).

Groups A and B were similar for disease duration and quality of metabolic control evaluated by HbA_{1c}. HbA_{1c} was 7.4 ± 2.1 and 7.9 ± 2.5% in groups A and B, respectively. HbA_{1c} was measured by high-pressure liquid chromatography (Bio-Rad Richmond, CA). AER was analyzed by radioimmunoassay (Pharmacia, Uppsala, Sweden) (19).

Fluorescein angiography was performed with a Kowa RC-XF fundus camera after quick injection of 2 ml of 20% sodium fluorescein into the antecubital vein. Angiograms were taken with ASA400 black-and-white film.

Static perimetry was performed using the 24-2 program of a modified Humphrey Field Analyzer 640 (Humphrey Instruments, San Leandro, CA). The test was performed in both eyes. Evaluated visual field parameters were foveal threshold and mean sensitivity for both achromatic and blue-on-yellow perimetry. In addition, a subdivision of the visual fields was performed as previously described (5).

For achromatic perimetry, the parameters used were background luminance, 31.5 apostilb; stimulus size, Goldmann III; and stimulus color, white.

The background illumination was extinguished using standard Humphrey software. A bright yellow background of 80.9 cd/m^2, producing a retinal illuminance of ~2.8 photopic trolands was produced using a carousel projector mounted on the left side of the perimeter cabinet as suggested by Sample and Weinreb (15). Wratten #12 filters were placed in front of all background sources to produce a yellow background. Then we adjusted and calibrated the background until it displayed equal luminance across the central 30° of the visual field. A filter holder was placed in the stimulus light path just behind the perimeter's shutter box, and a 440-nm interference filter (half-bandwidth of 4 nm) was inserted into the holder (15). The modifications for blue-on-yellow perimetry became operative after the instrument had performed its standard internal calibration routine.

Mean perimetric sensitivity was evaluated for each group (normoalbuminuric and microalbuminuric), for each area, and for each test (achromatic and blue-on-yellow perimetry). Furthermore, mean retinal differential sensitivity (e.g., algebraic difference between mean blue-on-yellow perimetry and mean achromatic perimetry) was determined.

All data are presented as means ± SD. For statistical analysis, the average of the values found in the two eyes was evaluated. Statistical analysis was performed with an SPSS software package (release 6.0; Chicago, IL). A normal distribution of data was found in both groups for each test. Intergroup analysis was performed with one-way analysis of variance (ANOVA); intragroup variations were evaluated by ANOVA for repeated measures: the multiple range tests were performed with the Duncan test. Linear regression analysis and Pearson correlation coefficients were used to evaluate the relationship between AER and perimetric mean sensitivity (achromatic, blue-on-yellow, and mean differential sensitivity). The level of significance was set at $P < 0.05$.

RESULTS

Central color vision

At the beginning of the study, all groups showed normal age-corrected TES values. No significant differences between mean TES values of diabetic subgroups (group A: 109.27 ± 51.27; group B: 105.95 ± 49.59) and control subjects (98.54 ± 35.92) were found.

Achromatic perimetry

No differences were found between diabetic subgroups and control subjects with regard to foveal threshold. Mean perimetric sensitivity was similar in the diabetic subgroups and control subjects (Table 1). Analysis of subareas of the visual field showed no differences between diabetic subgroups with regard to subareas 1 and 2 (Tables 2 and 3), while a significant difference between the same subgroups was found in area 3 of the visual field ($P = 0.027$) (Table 4).

Blue-on-yellow perimetry

No significant differences between diabetic subgroups and control subjects were found with regard to foveal threshold. Microalbuminuric patients showed lower values of the mean perimetric sensitivity than did normoalbuminuric ones ($P < 0.00001$) and control subjects ($P < 0.00001$) (Table 1). In all three of the perimetric subareas evaluated, the sensitivity was lower in microalbuminuric patients than in normoalbuminuric ones (Tables 2–4).

Blue-on-yellow versus achromatic perimetry

The difference between the perimetric tests performed with achromatic and with blue-on-yellow stimuli showed statistically significant data, with a stronger level of significance in areas 1 and 2 ($P < 0.00001$) than in area 3 (Tables 2–4): the latter also showed a significant difference, but with the lowest level of significance ($P = 0.033$) (Table 4).

A significant relation between AER and retinal sensitivity was found with both blue-on-yellow and achromatic perimetry ($P < 0.0001$). This relation was stronger with the blue-on-yellow mean perimetric sensitivity than with the achromatic one ($r = -0.80$ and $r = -0.61$, respectively).

Regression analysis showed a significant relation between AER and the retinal differential sensitivity between blue-on-yellow and achromatic perimetry ($P = 0.008$) (Fig. 1).

CONCLUSIONS — Our data suggest that diabetic children without fluorescein angiographic signs of retinopathy can have an impairment of achromatic and chromatic perimetry if they present persistent microalbuminuria. This observation is in agreement with data of other authors, who detected impairment in psychophysical tests in the absence of fluorescein angiographic signs of retinopathy (1–4). Our data also confirm the usefulness of achromatic perimetry in the detection of early retinal abnormalities in the absence of fluorescein angiographic signs of retinopathy, as previously reported (5,20).

Moreover, our study provides evidence that, although no significant difference between diabetic subgroups and control subjects was found with regard to central color vision (tested with Farnsworth 100 HUE) and foveal threshold (evaluated by both achromatic and blue-on-yellow perimetry), blue-on-yellow perimetry, evaluating short wavelength, seems to be more useful than achromatic perimetry in the detection of retinal impairment in diabetic microalbuminuric patients without fluorescein angiographic signs of retinopathy. In fact, we have studied diabetic children with persistent microalbuminuria who have already shown defects in the mid-periphery of the visual field by achromatic perimetry (5); by means of color perimetry, we not only confirmed the defects of the visual field detected by achromatic perimetry, but we also found more severe defects in the same areas. Further, when we tested with blue-on-yellow perimetry the areas of the visual field in which the achromatic perimetry showed no differences between control subjects and microalbuminuric and normoalbuminuric patients, we discovered other significant defects. In agreement with these data, we found that renal parameters had a stronger relation with blue-on-yellow mean perimetric sensitivity than with achromatic. Furthermore, the linear regression showed a significant relationship between AER and the retinal differential sensitivity between chromatic and achromatic perimetry. In our study, mean lens opacity in diabetic patients, as determined using the IntraOptics opacity lens meter, an accurate instrument for measuring lens changes (21), did not differ from that in control subjects. For this reason, data obtained in this study cannot be influenced by differences in light transmission through the lens.

This study is in agreement with other authors (15,22–26) who suggested that color perimetry is more useful and more sensitive than achromatic perimetry in the detection of preclinical visual defects in various diseases affecting the central visual field. To the best of our knowledge, this is the first study performed with blue-on-yellow perimetry in diabetic children. Our study has shown that in diabetic children with persistent microalbuminuria, the visual field defects are more severe than hitherto thought; in fact, by means of color perimetry, it is possible to detect a significant reduction in all the areas examined and not only in the mid-periphery of the

Table 2—*Mean sensitivity (in decibels) of area 1 tested with blue-on-yellow perimetry in diabetic subgroups and control subjects*

	Achromatic	Blue-on-yellow	Difference
Microalbuminuric (group A)	31.55 ± 1.42	18.90 ± 1.29	12.65 ± 0.25
Normoalbuminuric (group B)	31.60 ± 2.13	21.18 ± 1.64	10.43 ± 0.85
P value	0.925	<0.00001	<0.00001

Data are means ± SD.

Table 3—*Mean sensitivity (in decibels) of area 2 tested with blue-on-yellow perimetry in diabetic subgroups and control subjects*

	Achromatic	Blue-on-yellow	Difference
Microalbuminuric (group A)	28.92 ± 2.52	16.51 ± 1.56	12.41 ± 1.12
Normoalbuminuric (group B)	29.49 ± 1.72	19.10 ± 1.37	10.39 ± 0.74
P value	0.347	<0.00001	<0.00001

Data are means ± SD.

Table 4—*Mean sensitivity (in decibels) of area 3 tested with blue-on-yellow perimetry in diabetic subgroups and control subjects*

	Achromatic	Blue-on-yellow	Difference
Microalbuminuric (group A)	26.96 ± 2.33	16.00 ± 1.66	10.96 ± 1.08
Normoalbuminuric (group B)	28.76 ± 3.07	18.37 ± 2.99	10.39 ± 0.76
P value	0.027	0.002	0.033

Data are means ± SD.

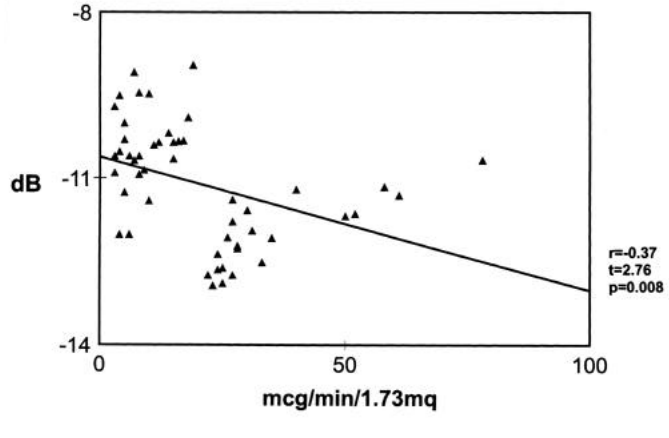

Figure 1—*Relationship between AER and blue-on-yellow/achromatic perimetry differential sensitivity (e.g., algebraic difference between mean blue-on-yellow perimetry and mean achromatic perimetry).*

visual field as we previously reported by achromatic perimetry (5).

Evidence for the blue-yellow deficit of central color vision function is often present in diabetic patients before the development of retinopathy (3,4,27). This suggests that the short wavelength–sensitive cones or their neural connections are more susceptible to damage from hyperglycemia than are the long wavelength– and medium wavelength–sensitive cone systems (15). The usefulness of blue-on-yellow perimetry may be due to the preferential stimulation of the blue (short wavelength–sensitive) pathway, the saturation of the green (medium wavelength–sensitive) and the red (long wavelength–sensitive) pathways, and to the high luminance level adapting the rod response (12,28). But regardless of the mechanism, we conclude that some eyes with IDDM exhibit normal central color vision and a normal central visual field when tested by achromatic perimetry but a reduced chromatic sensitivity when tested with blue-on-yellow perimetry, and we recommend this technique to complete the examination of the visual function of diabetic patients with persistent microalbuminuria.

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