COLOR VISION IN 42 CONGOLESE PATIENTS WITH TUBERCULOSIS RECEIVING ETHAMBUTOL TREATMENT

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ABSTRACT

Purpose: To study color vision in Congolese patients with tuberculosis receiving ethambutol therapy.

Methods: A prospective, descriptive study of color vision test in patients with systemic tuberculosis receiving ethambutol was performed between April 1995 and January 1998 at the Department of Ophthalmology, University of Kinshasa. Color vision tests were assessed with pseudoisochromatic plates (the Ishihara Pseudo-isochromatic Plates), the AO-HRR (American Optical Handy Rand Rittler), the Bölle and Kastel anomaloscope, Farnsworth-Munsell test (the D-15 and the FM-100).

Results: There were 42 patients with a mean age of 33 years (range, 14 to 75 years). The color vision of all the patients was found to be normal as measured by the Ishihara pseudoisochromatic plates. One (2%) patient showed color vision defect (anarchic axis] with the OA-HRR test. Three (7%) of 42 patients displayed blue-yellow color axis or anarchic axis color vision test on the D-15 test. Fifteen (36%) of 42 patients had high total error scores at the Farnsworth-Munsell 100 test. The color axis was as follows: anarchic axis (13.1%), red-green-color and blue-yellow-color combined axis (13.1%), blue-yellow color axis (7.5%). Results of the Bölle and Kastel anomaloscope were normal in all patients.

Conclusion: Our results confirm the importance of color vision examinations in the detection of the complications of ethambutol treatment.

RÉSUMÉ

But: Etudier la vision des couleurs chez les patients congolais tuberculeux sous éthambutol.

Méthodes: Une étude prospective, descriptive de la vision des couleurs chez des patients congolais tuberculeux traités a l'éthambutol a été réalisée d'avril 1995 à janvier 1998 au Département d'Ophtalmologie à l'Université de Kinshasa. L'examen de la vision des couleurs a été réalisé avec les tests suivants: Ishihara, AO-HRR, Panel D15, test de Farnsworth-Munsell 100 Hue et l'anomaloscope de poche de Bölle et de Krastel.

Résultats: Durant cette période, 42 patients ont été séléctionnés avec un âge moyen de 33 ans ±0.1 (limites, 14 à 75 ans). Aucun patient n'a manifesté une plainte en rapport avec la vision des couleurs. Au cours du suivi, le test de Ishihara a été normal chez tous les patients, le test de OA-HRR a montré une dyschromatopsie non sytématisée chez une patiente (2%). Le Panel D15 a montré une dyschromatopsie d'axe bleu-jaune ou anarchique chez 3 patients (7%). Le test 100 Hue a montré une dyschromatopsie chez 15 (36%) lors du suivi. Les résultats avec l'anomaloscope de Bölle et de Krastel ont été normaux chez tous les patients.

Conclusion: Notre étude confirme l'importance des tests de vision de couleur dans le suivi des malades tuberculeux traités à l'éthambutol.

KEY-WORDS

Ethambutol. Tuberculosis. Color vision tests.

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MOTS- CLÉS

Ethambutol. Tuberculose. Test de vision des couleurs.

INTRODUCTION

Ethambutol is a tuberulostatic agent which is effective against *M. tuberculosis* and is well documented to cause ocular symptoms of reduced visual acuity, changes in color vision, and visual field loss [2-4, 7-12,14,18].

Optic neuropathy is the side effect concerning mostly the ophthalmologist. Neuropathy can occur in an axial or periaxial pattern [2-4,7-12,14,18]. The incidence of this reaction is dose-related and is observed in 15% of patients receiving 50 mg/kg/day, in 5% of those receiving 25 mg/kg/day, and less than 1% of those taking 15 mg/kg/day or less [1-5, 7,8].

The periaxial type is more often associated with visual field defects, paracentral scotomas with normal vision and normal color perception. With axial involvement, green color vision testing loss is more common than red loss. Symptoms of optic neuritis generally become only evident 3 to 6 months after starting the drug. Although the mechanism by which ethambutol causes retrobulbar neuritis is largely unknown [6], van Dijk and Spekreijse [21] and Kakisu and associates [16] have suggested that ethambutol may affect the amacrine and bipolar cells of the retina since color vision can be affected without altering visual acuity.

The objective (goal) of this study is to report our findings in using color vision tests to ascertain whether we could detect any color vision disturbances in patients treated for tuberculosis with ethambutol and who apparently have normal vision.

PATIENTS AND METHODS

Patients

This prospective and descriptive study was done between April 1995 and January 1998 at the Department of Ophthalmology, University of Kinshasa. Seventy-seven patients with systemic tuberculosis receiving ethambutol were referred to us by the Department of Medicine. Before receiving ethambutol and entering in the study, patients were informed of the purpose of the study and provided verbal consent to participate.

Each patient had a complete eye examination. This consisted of history pertaining to past ocular disease, visual acuity, external examination of the eyes and adnexae, muscle balance and pupil reflex, refraction, fundus examination, measurement of intraocular pressure, visual field examination and color vision test.

All eligible patients were required to have at least 7/10 best-corrected visual acuity to see the color plates. In addition, patients were excluded if they had any condition that may possibly contribute to color vision defects. These conditions included systemic and local retinopathy such as diabetic retinopathy, sickle cell retinopahy, central serous retinopathy, retinitis pigmentosa, previous retinal detachment, optic neuropathies such as glaucoma, optic neuritis or optic atrophy, cataract with more than +2 nuclear sclerosis, known congenital color defects and medications such as digitalis, oral contraceptives and indomethacin [13].

Of 77 examined patients, 35 were excluded and 42 constituted our study group. Of these 42 patients, 28 (67%) had pulmonary tuberculosis, 10 (24%) extra pulmonary tuberculosis and 4 (9%) a combined form of tuberculosis. All received ethambutol (25 mg/kg body weight/day for a period not exceeding 2 months), followed by a maintenance dose of 15 mg/kg/day together with isoniazid (300 mg daily), rifampicin (600 mg daily) and B-complex capsules. Table 1 summarizes the clinical profiles of the patients. The diagnosis of tuberculosis was made by the internist.

Patients were examined prior to and followed while on ethambutol. They were followed-up for at least 8 months (at intervals of approximately two weeks) with the parameters of clinical examination, including vision recording, color vision and visual field examinations.

Table 1: *Characteristics of patients with tuberculosis receiving ethambutol*

N	42
Age (years)	
mean age±SD	33±1
range	15-75
Gender	
male	21
female	21
Eyes	
right eye	41
left eye	42
Tuberculosis (form)	
pulmonary	28
extra-pulmonary	10
mixed	4

Examination and Color vision testing

Color vision tests were administered by one of us (BZA) and under monocular viewing conditions. None of the patients had any previous experience with the tests. Both eyes were examined for each patient.
Color vision tests were assessed with pseudoisochromatic plates (the Ishihara Pseudo-isochromatic Plates), the AO-HRR (American Optical Handy Rand Rittler), the Bölle and Kastel anomaloscope, Farnsworth-Munsell test (the D-15 and the FM-100).

Electrophysiological examination (visual evoked response) was not performed because unavailable.

Analysis

Specific "failing" criteria for each test are listed in Table 2. We determined the Rayleigh equation in both eyes of each patient, using the Bölle and Kastel anomaloscope. For the Rayleigh equation, green (545 nm) and red (670 nm) primaries were mixed to produce a yellow (589 nm). The D-15 was scored using two or more major crossings as a failure.

Table 2: *Failing criteria for color vision tests*

Test	Failing criteria
Ishihara	≥ 2 errors on color plates
AO - HRR	Any error on screening plates supported by similar errors on diagnostic plates
D-15	≥ 2 major crossings
100-Hue	> mean error score + 2 SD mean error score (according to age group)

For the Farnsworth-100 Hue, each eye was tested separately and the error scores were calculated as described by Verriest [22]. Error scores of patients with tuberculosis receiving ethambutol were compared with scores of aged-matched normal subjects as previously reported by Kaimbo et al [15]. Patients who scored higher than 2 SD above the mean error on the test were considered as having a color vision test defect.

Patients were considered to have a color vision defect if they failed at least one of the color vision tests. The type of color defects was classified as blue-yellow (BY), red-green (RG), or mixed BY-RG defect (mixed). Because of expected high correlation between both eyes of each patient, data from only one eye were analyzed.

Statistical analysis (Student's t-test, chi-square test; $P \leqslant 0.05$ rejection level) did not reveal any significant difference in age, type (form) of tuberculosis or duration of ethambutol use between the two sexes.

RESULTS

No patient included in this study had any vision color eye complaints. The color vision of all the patients was found to be normal as measured by the Ishihara pseudoisochromatic plates. One (2%) patient showed color vision defect [anarchic axis] with the OA-HRR test during the follow-up period. Three (7%) of 42 patients displayed blue-yellow color axis or anarchic axis color vision test on the D-15 test. Fifteen (36%) of 42 patients had high total error scores at the Farnsworth-Munsell 100 test. The color axis was as fellows: anarchic axis (13.1%), red-green-color and blue-yellow-color combined axis (13.1%), blue-yellow color axis (7.5%). Color vision defects appeared several months (mean, 5 months) after ethambutol therapy was begun. Results of the Bölle and Kastel anomaloscope were normal in all patients. The mean Rayleigh for all patients was 5.56 ±0.73 (range, 4 to 8.8).

Ethambutol was stopped during the follow-up period in three patients because they developed total color blindness. After discontinuation of drug therapy, two of them recovered color vision and in one neither the visual acuity nor the color vision improved.

DISCUSSION

In this study, we examined the results in color vision tests in patients with tuberculosis receiving ethambutol. Overall, 15 (36%) out of 42 patients showed color vision defects. Red-green, blue-yellow or combined defects and anarchic axis were observed. These results support previous studies that demonstrated blue-yellow errors in early stage of intoxication and blue, red-green or tritanomalous defects in a later stage of intoxication in patients treated with ethambutol. These changes in color vision can occur even before visual acuity and visual fields are affected. Color vision disturbances are probably the most sensitive indicator of early ethambuol optic neuropathy [19].

In our patients, color vision disturbances were detected after five months of ethambutol treatment. Signs of ocular toxicity can appear as early as several weeks following initial therapy, but the onset of ocular complications usually occurs several months after therapy is begun [1,17,20].

In this study, three patients developed total color blindness and ethambutol therapy was discontinued. One of them didn't recover visual acuity and color vision. In intoxication with ethambutol, once changes have occurred in visual acuity, visual field, or color vision, these functional disturbances may further deteriorate even after ethambutol has been discontinued [5]. More often, however, there is recovery of pretreatment visual acuity and visual field several months or years following discontinuation of drug treatment [7,8]. The degree of recovery depends largely on the extent to which ethamutol has compromised optic nerve function, and if the ocular toxicity is not recognized early, the drug can cause permanent loss of vision [23].

In this study, the Farnsworth-Munsell 100 Hue detected color vision abnormalities in 36% of cases whereas the results were normal with Ishihara test and the Bölle and Kastel anomaloscope, and abnormal in only 2% and 7% with the AO-HRR and Panel D-15 tests respectively. The standard pseudoisochromatic plates screening test doesn't seem to be useful in clinical practice. The Farnsworth-100 Hue seemed to be more sensitive.

Our results confirm the great importance of color vision examination in the detection of complications after ethambutol treatment.

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