Visual Field Changes in Patients Receiving Antitubercular Drug Therapy at Tertiary Care Hospital: An Analytical Observational Study

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ABSTRACT

Introduction: Tuberculosis is a worldwide public health problem. The antitubercular drugs which affect the optic nerve are isoniazid and ethambutol. The ethambutol induced toxic optic neuropathy is quite common while that induced by isoniazid is rare. Sudy aimed to evaluate visual field changes in tubercular patients with DOTS therapy (directly observed treatment short course).

Material and Methods: A prospective clinical study was conducted on 100 patients suffering from tuberculosis attending the DOTS centre of Government Medical College and Associated hospitals, Srinagar. The patients were evaluated for visual field changes after exposure to DOTS therapy over a period of time.

Results: In the present study of 100 patients, 198 eyes were examined. It was found that 13.63% eyes developed changes in visual fields after the two months exposure of DOTS therapy. When the therapy was stopped for two months, 66.66% eyes showed improvement in their visual field. The most common defect seen among such patients were peripheral defects in different quadrants (8.1%).

Conclusion: In the present study we concluded that ethambutol therapy in tubercular patients, when taken according to the recommended dose and duration, can cause ocular toxicity in the form of visual field changes. Significant number of patients showed an improvement in visual field after cessation of therapy.

Keywords: Tuberculosis, Ethambutol, Visual Field, Perimetry

INTRODUCTION

Tuberculosis is a common and in many cases lethal infectious disease caused by various strains of mycobacterium, usually Mycobacterium Tuberculosis. Tuberculosis usually affects lungs, but can also affect other body parts in the form of extrapulmonary tuberculosis.[1]

DOTS stands for "Directly Observed Treatment Short Course" and is a major plank in the WHO Global Action Plan to stop tuberculosis. The first line anti-tubercular drugs are: isoniazid, rifampicin, pyrizinamide and ethambutol.

Ethambutol, a bacteriostatic drug, is given in the dose of 15-30 mg/kg. The incidence of ethambutol induced toxic optic neuropathy is in the range of 0.62% to 63% according to different studies. The incidence is directly proportional to the dose and duration of ethambutol therapy.

Optic neuropathy is the most important potential side effect of ethambutol manifesting as retrobulbar neuritis. The toxic optic neuritis may be of early onset or late onset, may be reversible or irreversible and axial or peri-axial.[2,3]

Affected individuals may complain of progressive, painless, visual blurring, central vision being commonly affected. Decreased colour perception may also be experienced. Dyschromatopsia (abnormal colour perception) may be the earliest sign of toxicity, classically documented to be red-green colour changes.[4,5]

Central defect is the most common visual field defect, but bi-temporal defects or peripheral field constrictions have also been reported. Perimetry is one way to systematically test the visual field. It is the systematic measurement of sensitivity in the visual field by the detection of presence of tests targets on a defined background. Automated perimetry is most commonly used in clinical practice.[6-9]

AIM and objectives were to evaluate the visual field changes in tubercular patients with DOTS therapy, to evaluate the reversibility of these side effects after the discontinuation of the therapy.

MATERIAL AND METHODS

The prospective analytical hospital based study was conducted on 198 eyes of 100 patients (two patients were one-eyed) suffering from tuberculosis attending the DOTS centre of Government Medical College, Srinagar after approval from the Hospital Ethical and Research board. The study was conducted from January 2014- June 2015.The patients were studied on the basis of any changes in their visual fields after consumption of DOTS therapy over a period of time.

Inclusion Criteria: All new tubercular patients on DOTS therapy.

Exclusion Criteria: Patients with history of tubercular meningitis, renal diseases, past history of use of anti-tubercular therapy, history of vasculitis, demylenating diseases, other causes of optic neuritis (syphilis, measles) and optic disc oedema.

Detailed ocular history and relevant medical/surgical history was recorded in all cases. General physical and systemic examination was conducted on all the cases. Ocular examination included: best corrected visual acuity, colour vision, contrast sensitivity, intraocular pressure record, slit lamp bio-microscopy, fundus examination and visual fields.

The patients were evaluated before starting the therapy, at the end of two months of therapy and then after two months of cessation of therapy.

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Colour vision testing was done using Ishihara chart.

Patients were analysed on Humphrey field analyser for visual field changes, after taking proper consent. Humphery field analyzer (HFA) uses the normal testing distance of 30cm. Ambient light source should be dim. Patient's chin is placed on position chin holder. Full refractive correction should be used in patients with existing refractive errors. One eye is tested at a time (mono ocular test), whereby the other eye is occluded. The eye is centered in crosshairs of eye position monitor. The patient is made comfortable with the button in the dominant hand, while the hand is supported on the table.

The test is started by presenting four primary points one in each quadrant. It assumes the blind spot location and maps it only if patient misses the periodic fixation test. The fixation is monitored by both the corneal reflex method and a television view of the patient's eye. The HFA uses two systems for monitoring patient fixation- the standard Heijl-Krakau periodic blind spot monitoring and the IR Gaze Tracking System.

The patient is asked to look in the centre of the green fixation mark. Lights will flash up in different places. The patient is asked to push the button in his hand, whenever he sees a light. If the patient needs a break, the response button is kept pushed. The instrument will continue when the button is released. The test is repeated in a similar way in the other eye.

Age (years)	No.	%age	Mean±SD	Range
≤ 30	35	35%	39.1±15.54	10-65
31-40	16	16%		
41-50	17	17%		
≥ 51	32	32%		
Total	100	100%		
Gender	**No. of Patients**		**No. of Eyes**	
	No.	**%age**	**No.**	**%age**
Male	62	62%	122	61.6%
Female	38	38%	76	38.4%
Total	100	100%	198	100%

Table-1: Age and Gender distribution of patients

STATISTICAL ANALYSIS

Statistical Software SPSS (VERSION 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Mc Nemar Chi-square test was employed to compare changes in visual function in the studied eyes. P- value less than 0.05 was considered statistically significant.

RESULTS

Mean age of the patients was 39.1 ± 15.54 years.

Out of 100 selected patients 62 (62%) were males and 38 (38%) were females.

On using Mc Nemar Chi-Square Test these differences of visual acuity between baseline and at two months from baseline ($P < 0.000004$), and between baseline and after two months of cessation of therapy ($P < 0.000002$) was statistically significant. These differences in color vision status between baseline and at two months from baseline ($P < 0.000001$), and between baseline and after two months after cessation of therapy ($P < 0.000004$), are statistically significant.

In our study of 198 eyes of 100 patients, there was no visual field change at baseline (as already excluded from the study). At the end of two months it was seen that 27/198 (13.63%) eyes

Visual Acuity	Baseline		Two months from BL		Two months after cessation of therapy	
	No.	%age	No.	%age	No.	%age
6/6	198	100	179	90.4	181	91.4
6/9-6/12	0	0	14	7.1	14	7.1
6/18-6/24	0	0	3	1.5	2	1.0
6/36-6/60	0	0	2	1.0	1	0.5
Total No. of affected eyes			19	9.6	17	8.6

Table-2: Visual acuity in studied eyes

Color Vision	Baseline		Two months from Baseline		Two months after cessation of therapy	
	No.	%age	No.	%age	No.	%age
Blue-Yellow Color Defect	0	0	12	6.1	6	3.0
Blue Defect	0	0	12	6.1	6	3.0
Red-Green Defect	0	0	3	1.5	3	1.5
Red defect	0	0	4	2.0	4	2.0
Red-Blue-Green	0	0	0	0.0	0	0.0
Total eyes affected	0	0	31	15.7	19	**9.5**

Table-3: Color vision changes in studied eyes

Perimetry	Baseline		Two months from Baseline		Two months after cessation of therapy	
	No.	% age	No.	% age	No.	% age
Central Scotoma	0	0	4	2.0	4	2.0
Centro ceacal Scotoma	0	0	0	0.0	0	0.0
Peripheral Constriction	0	0	6	3.0	6	3.0
Peripheral defects in different quadrants	0	0	15	7.6	14	7.1
Bi-temporal Hemianopea	0	0	2	1.0	0	0.0
Total eyes affected	0	0	27	13.6	24	**12.1**

Table-4: Visual field changes in studied eyes

developed changes in their visual fields. The most common defect seen was the peripheral defects in different quadrants 15/198 (8.1%) eyes. Other defects seen were peripheral constriction of the isopter in 6/198 (3.03%) eyes, central scotoma in 2 (1.01%) eyes and bitemporal hemianopia was seen in 2 (1.01%) eyes. After two months of cessation of therapy 24/198 (12.1%) eyes were those that had visual field defects.

It was found that after two months of cessation of therapy 18/24 (66.66%) eyes showed some improvement in their visual field status. 6/27 (22.22%) eyes showed no improvement while 3/27 (11.11%) eyes showed a complete recovery.

These differences in visual fields at two months from baseline ($P < 0.000001$) and after two months of cessation of therapy ($P < 0.000001$) are statistically significant.

DISCUSSION

Out of 100 patients with 198 eyes, at baseline visual acuity ranged from 6/6 (198 eyes)-6/60 (2 eyes; these 2 eyes were excluded from the study as all the tests conducted on the affected eyes were not applicable to these 2 eyes because of very low baseline vision). At the end of two months i.e; first follow up, a decreased visual acuity was seen in 21/198 eyes (10.6%). After two months of cessation of therapy the decreased visual acuity was seen in 19/198 eyes (9.6%). On using Mc Nemar Chi-Square Test these differences of visual acuity between baseline and at two months from baseline ($P < 0.000004$), and between baseline and after two months of cessation of therapy ($P < 0.000002$) was statistically significant. It was observed that after 2 months of cessation of therapy 10/19 (52.6%) eyes had an improved status of visual acuity, while 2/19 (10.5%) showed a complete recovery to baseline. It was also seen that 5/19 (26.3%) eyes had a same status, while 2/19 (10.5%) eyes showed a worsening of visual acuity status after 2 months of therapy cessation. Garg P et al (2015)[10] in their prospective study of ocular toxicity of ethambutol evaluated 64 patients. Their baseline visual acuity ranged from 6/6 – 6/60. Visual acuity loss was seen in 6/126 eyes and this difference in visual acuity between the baseline and second month after start of therapy was statistically significant ($P <0.001$). It was seen that all the affected 6 eyes improved on stoppage of the drug after a follow up of 1-2 months.

In our study of 198 eyes of 100 patients, it was observed that a total of 46/198 (23.23%) eyes had an altered color vision status at two months of follow up. Of these affected eyes, maximum number showed a blue-yellow defect 12/31(42%), and blue defect in 12/31 (42%) eyes. Red defect was seen in 4/31 (13%) eyes and 3/21 (9.67%) eyes showed red-green defect. After two months of cessation of therapy color vision changes were seen in 19/198 (9.5%) eyes. These differences in color vision status between baseline and at two months from baseline ($P< 0.000001$), and between baseline and after two months after cessation of therapy ($P< 0.000004$), were statistically significant. It was observed that after two months of cessation of therapy 12/31 (38.7%) eyes showed improvement in color vision status, while 19/31 (15.65%) eyes illustrated no changes. Garg P et al (2015)[10] evaluated 126 eyes of 64 patients and found a total of 16 eyes of 8 patients who developed color vision abnormalities. Out of these, 4 eyes showed red-green color defects, while others showed blue-yellow color impairment. The difference of color vision was statistically significant ($P=0.003$).

In our study there was no visual field change at baseline (as already excluded from the study). At the end of two months it was seen that 27/198 (13.63%) eyes developed changes in their visual fields. The most common defect seen was the peripheral defects in different quadrants 15/198 (8.1%) eyes. Other defects seen were peripheral constriction of the isopter in 6/198 (3.03%) eyes, central scotoma in 2 (1.01%) eyes and bitemporal hemianopia was seen in 2 (1.01%) eyes. After two months of cessation of therapy 24/198 (12.1%) eyes were those that had visual field defects. These differences in visual fields at two months from baseline ($P < 0.000001$) and after two months of cessation of therapy ($P <0.000001$) were statistically significant. It was found that after two months of cessation of therapy 18/24 (66.66%) eyes showed some improvement in their visual field status. 6/27 (22.22%) eyes showed no improvement while 3/27 (11.11%) eyes showed a complete recovery. Kho Richard C et al (2011)[11] studied 38 eyes of 19 cases with ethambutol induced optic neuropathy. They demonstrated that 36/38 (95%) eyes showed a visual field loss worse in temporal hemifields, 31/38 (82%) eyes showed some degree of margination along the vertical midline of which 26 had superimposed central/centroceacal scotomas. 12/38 (32%) eyes revealed bitemporal visual field loss marginating along the midline. They found in their study that a visual improvement on automated perimetry occurred in 27/34 (79%) eyes after discontinuing the ethambutol (mean time=15.7 months). Garg P et al (2015)[10] in their prospective evaluation of ocular toxicity in patients receiving ethambutol found that 8 eyes of 4 participants (6.3%) showed visual field defects after two months of ethambutol intake. Visual field changes noted had a statistical significance of 0.0412 by Mc Nemar Chi Square Test. 1 participant showed centroceacal scotoma while remaining eyes showed peripheral constriction (bilateral in all). Menon V et al (2009)[12] in their prospective evaluation of visual function for ethambutol toxicity studied 104 eyes of 52 patients being treated with ethambutol and observed that visual field defects developed in 8/104 (7.6%) eyes upon follow up. It was also seen that there was a reversal of this observed toxicity in visual fields in 80% eyes after one month of stoppage of ethambutol. Goyal JL et al (2003)[13] in their prospective evaluation of visual functions in patients on ethambutol studied a total of 60 eyes of 30 patients receiving ethambutol as a part of their ATT and the patients were examined on monthly basis. They noted that 3/30 (10%) patients developed visual field defects. After cessation of treatment visual recovery was complete in only 1 patient and partial in 2 patients.

CONCLUSION

In our present study we conclude that ethambutol therapy in tuberculosis, when taken according to the recommended dose and duration, can cause ocular toxicity. This ocular toxicity manifests in the form of changes in visual acuity, color vision, visual fields, and funduscopic picture. It was also observed that a significant number of patients show an improvement after cessation of therapy.

We recommend that tuberculous patients receiving ethambutol therapy should have an ophthalmic examination before the start of the therapy and then periodically during the course of therapy. There is a need of compulsory education to the patients

about blurring of vision, problems in appreciating different colors and any non-seeing areas in the field of vision. This will aid in an early modification of therapy as soon as the visual adverse effects ensue.

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