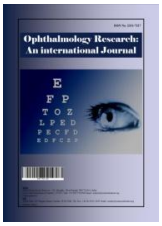

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The Effect of Anti-Tubercular Drugs on Retinal Nerve Fiber Layer Thickness Using Optical Coherence Tomography

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Authors' contributions

This work was carried out in collaboration between both authors. Authors PKS and Prasnnta designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors PKS and Prasnnta managed the analyses of the study. Author Prasnnta managed the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Purpose: To study the effect of anti-tubercular drugs on retinal nerve fiber layer (RNFL) thickness using optical coherence tomography.
Methods: The study was done in thirty patients newly diagnosed with pulmonary tuberculosis which were given anti-tubercular treatment (isoniazid, rifampicin, ethambutol and pyrazinamide) at DOTS centre of K. N. TB and Chest hospital (Dr. S.N M C.) Jodhpur. Visual function tests (visual acuity, contrast sensitivity, color vision) and OCT assessment of RNFL done before initiation of treatment and after two month of treatment.
Results: After two months, RNFL thinning was present in 3 eyes out of total 60 eyes in temporal and superior quadrant.
Conclusion: The study revealed that the first line antitubercular drug Ethambutol causes RNFL thinning within two months of initiation of drug in the recomonded dose. In the initial stage of optic nerve toxicity, there are no clinically significant changes seen on posterior segment ophthalmoscopic examination and fundus photography.OCT can find out the retinal nerve fiber layer thinning even if there are minute changes.

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Keywords: RNFL; antitubercular drugs; OCT; pulmonary tuberculosis.

1. BACKGROUND

Tuberculosis is a major health problem worldwide. Globally, around 10 million people fall ill with TB every year. According to WHO report of 2019, India accounted for highest number of total TB cases in the world (27%), followed by china (9%), Indonesia (8%), Philippines (6%), and Pakistan (6%) [1]. The first line agents used for treatment of tuberculosis are isoniazid, rifampicin, ethambutol and pyrazinamide and the route of administration is oral. The recommended adult daily dose is 15 mg/kg of ethambutol and 5 mg/kg for isoniazid [2]. The most common anti-tubercular drug causes optic nerve toxicity is ethambutol. Isoniazid induced optic neuropathy is rare [3]. The ethambutol induced optic neuropathy in tuberculosis cases who received ethambutol was found in about 1% cases that is correlated to the dosage [4]. Thetoxicity of ethambutol is due to its chelating action which causes depletion of metal ions(zinc) in eye that leads to mitochondrial dysfunction in retinal ganglion cells. The most common involved retinal nerve fibers are papillo- macular bundal because of their high mitochondrial content [5,6]. Clinical signs of optic neuropathy are decreased colour and contrast sensitivity with central visual field defect [7,8,9].

Based upon principle of low coherence interferometry, Optical coherence tomography (OCT) is a non contact, non invasive newer diagnostic modality that provide high-resolution images of cross-sectional cuts of retina [10].

Therefore the purpose of this study was to determine the possible changes in retinal nerve fiber thickness due to optic nerve toxicity associated to Ethambutol by using Optical coherence tomography in the patients reveiving antitubercular treatment. Other diagnostic tools like Ishihara chart and Amsler grid were also used.

2. MATERIALS AND METHODS

The study was done on total 60 eyes of 30 patients newly diagnosed with pulmonary tuberculosis at DOTS centre of K.N.TB and Chest hospital (Dr. S.N M C.) Jodhpur and planned for initiation of DOTS regimens including ethambutol and isoniazid (fixed dose combination). Study period was from January 2020 to march 2020. Patients of age group 20-65, nonalcoholic and with no co-morbidities were included. Patients with visual acuity less than 6/36, corneal/lens opacities with no good results on OCT, defective color vision, glaucomatous changes and eyes with RNFL defect were excluded from the study.

After taking a detailed personal history, medication history, ocular history (color blindness), ophthalmic evaluation was done prior to starting DOTS treatment and after two month of treatment. The ophthalmic examination included: best corrected visual acuity by Bailey-Lovie type chart, contrast sensitivity test by contrast charts, color vision using Ishihara charts, Amsler grid test and posterior segment examination by indirect ophthalmoscopy and retinal nerve fiber thickness measurement by OCT.

2.1 RNFL Thickness Measurement

RNFL thickness in every quadrant was measured by SD-OCT(spectral domain- OCT).

Patients were evaluated again after two month of DOTS treatment. The pre- treatment OCT values of RNFL thickness were considered as baseline. Only high quality OCT scans were used.

3. RESULTS

There were 60 eyes of 30 patients studied in the two month period, out of which 25 patients were male(83.33%) and 5 patients were female(16.66%). Patient's body weight was also measured to get a more accurate dosage received according to weight. The mean age of patients was 40 year ranging from 20 to 65 year old (median 39 year old)). Visual acuity was found 6/6 to 6/36 but there were no visual disturbance seen after two months in any subject. Amsler grid test and color vision was also normal in all subjects. One patient had decreased contrast sensitivity. RNFL thinning was present in 3 eyes(two eyes of one patient and one eye of another patient) in temporal and superior quadrant.

Table 1. RNFL changes in 3 eyes

Eye	Quadrant	RNFL thickness before treatment	RNFL thickness after treatment
Eye 1	Temporal	87	76
	Superior	152	141
Eye 2	Temporal	91	83
	Superior	159	148
Eye 3	Temporal	84	73
	Superior	161	147

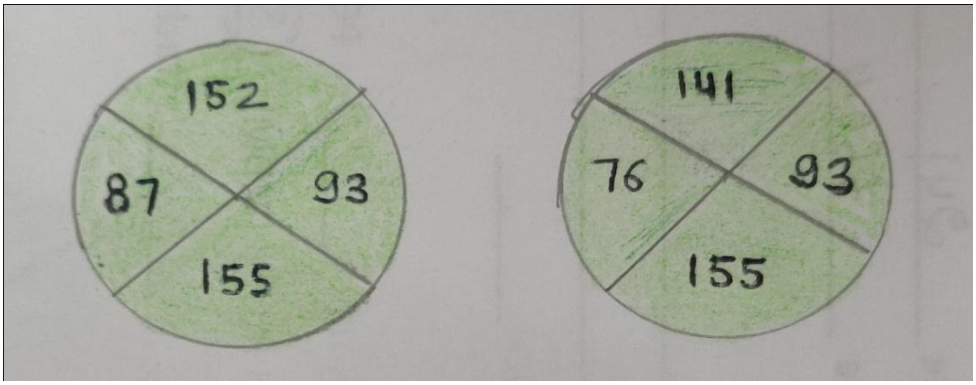

Fig. 1. RNFL measurement pre and post treatment

4. DISCUSSION

Ethambutol was used for treatment ofTuberculosis since 1961 and after WHO guidelines 2009, added in standard treatment of newly diagnosed activeTB cases [11,12]. Clinical features of ethambutol toxicity are decreased color and contrast sensitivity with defect in central vision. Symptoms usually begin after 4 months to one year of treatment, but sometimes can appear within few days of initiation of treatment [13]. Fundus with Indirect ophthalmoscopy is normal in early optic neuropathy, so studies that find out side effects of ethambutol and diagnostic modalities which can be used for early diagnosis of optic nerve toxicity are needed for preservation of visual functions.

In this two month duration of the study, the visual acuity of all patients was stable this can be explained with the previous study which declared that symptoms of optic neuropathy occur after 4 month of treatment (rarely before 2 month) [13]. The most common involved retinal nerve fibers are of temporal and superior region that papillo-macular bundal because of their high mitochondrial content [5,6]. Some authors proposed that side effect of ethambutol are reversible, [11] but other Studies [14] have found that vision loss occur even after stoppage of ethambutol treatment. OCT analysis of retinal nerve fibre layer can be used to diagnose ethambutol toxicity before clinical symptom or signs appear [15].

5. CONCLUSION

The study revealed that the first line antitubercular drug Ethambutol causes RNFL thinning within two months of initiation of drug in the recomonded dose. In the initial stage of optic nerve toxicity, there are no clinically significant changes seen on posterior segment ophthalmoscopic examination and fundus photography. OCT can find out the retinal nerve fiber layer thinning even if there are minute changes.

CONSENT

As per international standard informed and written participant consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard written ethical permission has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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