



EVALUATION OF THE EFFECT OF ETHAMBUTOL USAGE ON THE RETINAL NERVE FIBER LAYER USING SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY (SD-OCT)

Ophthalmology

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ABSTRACT

Objectives: The aim of this study was to use spectral-domain optical coherence tomography (SD-OCT) to evaluate the long-term effect of ethambutol on the optic nerve fiber layer. **Methods:** Sixty six eyes of 33 patients who had been treated with ethambutol for tuberculosis were retrospectively evaluated. Retinal nerve fiber layer (RNFL) analyses performed on old and newly diagnosed patients with tuberculosis were included in the study. Data of visual acuity, fundus examination, other diseases, and drug use history of all of the participants were evaluated. Color vision was tested with the Ishihara Color Test. Superior, inferior, nasal, and temporal quadrant RNFL parameters were evaluated using SD-OCT. **Results:** According to our all calculated z value mentioned, all= 0.05 are greater than the critical value of z. Therefore, we are rejecting our null hypothesis and highly significant p value support our alternative hypothesis. From this statistical significance result, our study can infer that there is no possibility of RNFL thinning in TB patients taking ethambutol for short period of time. **Conclusion:** We displayed that patient receiving TB medications, which were the basic medicines of anti-tubercular treatment, didn't experienced thinning in RNFL after the treatment period

KEYWORDS

Ethambutol, optical coherence tomography, optic neuropathy

INTRODUCTION

Tuberculosis that is caused by Mycobacterium is one of the most important systemic infections around the world.^[1] Ethambutol is a first-line medication that is used to treat infection by Mycobacterium species, particularly Mycobacterium tuberculosis and non- tubercular infections like M. avium complex and M. kansasii. However, it can lead to side effects including problems with vision, liver problems, and allergies.^[2] Ethambutol-induced optic neuropathy (EON) is a well-known complication arising from the use of ethambutol, the severity of which is in a dose-dependent manner. The toxicity is usually reversible on discontinuation of the therapy.^[3] However, there have been several reports of permanent damage to the visual function.^[4,5] The clinical characteristics of EON include painless loss of central vision andcecocentral scotomas in the visual field.

The prevalence of EON in patients treated for tuberculosis is estimated to be 1-2%.^[6] According to the World Health Organization (WHO), there are around 9.2 million new cases of tuberculosis each year, 55% of which will take ethambutol. , Given that the incidence of EON is about 1-2% among treated patients, these statistics suggest there could be as many as 100,000 new cases of EON annually.^[7] Furthermore, the risk of EON is highly dose dependent. The estimated prevalence of EON for ethambutol doses of ≤ 15 , 20, 25, and > 35 mg/kg per day are $< 1\%$, 3%, 5-6%, and 18-33%, respectively. At any of the therapeutic antimicrobial dosing regimens, there is a variable and sometimes idiosyncratic risk for EON and thus there is effectively no truly "safe" dose for EMB. Other than ethambutol dosage, risk factors for EON include age greater than 65 years and hypertension. Because ethambutol is excreted by the kidneys, renal disease can also increase the risk of optic neuropathy. Finally, multiple case reports have identified isoniazid, another first-line treatment for tuberculosis, as a cause of optic neuropathy similar to EON. Therefore, patients taking ethambutol in combination with isoniazid may be at increased risk for visual loss.^{[8][9][10]}

Pathogenesis

Retrobulbar optic neuropathy (normal appearing optic disc on presentation) is the most common form of EON.^[11] While the exact mechanism of the neurotoxic effect of EMB on the optic nerve is unknown, it is believed that the metal chelating effects of this drug may be responsible. One theory is that the chelation of copper disrupts oxidative phosphorylation, as there is less copper available in human mitochondria. Another theory is that the chelation of zinc inhibits lysosomal activation. Moreover, in animal studies on rat optic nerves,

zinc deficiency has been associated with destruction of myelin and glial cell proliferation, suggesting that there may be a similar effect in humans.^[12] In addition, prolonged EMB use has been shown to be associated with deficiencies in vitamin E and vitamin B1 which may exacerbate the optic neuropathy.

MATERIALS AND METHODS

Type Of Study: Observational study.

Study Design: Cross Sectional study.

Duration Of Study: 6 Months

Place Of Study: Study conducted in the department of ophthalmology at M.G.M Medical College & L.S.K. Hospital, Kishanganj, Bihar.

Study Period: August 2023 to February 2024

Source Of Data: Patients attending the Eye OPD of M.G.M Medical College & L.S.K Hospital under M.G University, with or without ocular complications of ethambutol induced optic neuropathy in one or both eyes during the study period will be taken up for the study.

Study Tools:

1. Snellen's Vision Chart
2. Pupillary response to light
3. Colour Vision – Ishihara chart
4. Autorefraction
5. Direct Ophthalmoscopy
6. Slit lamp biomicroscope Examination
7. Slit lamp biomicroscope Examination with 90D
8. Fundus photography

Inclusion Criteria:

1. **Disease-** Tuberculosis
2. **Sexes-** Both Sexes
3. Patients attending Eye OPD after taking treatment for TB from TB and Chest department in MGMMC
4. Giving informed consent to participate in the study.

Exclusion Criteria:

1. Any media opacity

Methodology

Informed consent will be obtained from each of participants prior to the examination. An examination proforma will be used to elicit information from respondents. Every consenting patient from the outpatient clinic who meet the inclusion criteria will be recruited into the

study between 2023-2024 till the required number of participants will be obtained. Old and newly diagnosed patients with Tuberculosis will be recruited into the study. Ocular history will be taken and ocular examination and further investigations will be carried out on each patient.

The patients will be examined clinically in the Eye OPD and then their Visual acuity, anterior segment examination by torch light method and Slit Lamp biomicroscopy will be done.

The posterior segment will be examined by direct ophthalmoscope and 90D lens. The fundus findings will be documented by fundus photography.

A Summary will be made, conclusions will be drawn and recommendations will be made.

Ethical Consideration

Permission will be taken from the ethical committee of M.G.M. Medical College & L.S.K. Hospital. Kishanganj, Bihar prior to the commencement of the study.

Analysis

The data collected will be entered into an Excel sheet. It will be subjected to statistical analysis in MS Excel and SPSS version 19.0. Data will be expressed in frequencies and percentages when qualitative and in mean $\pm$ SD when quantitative. Chi square test will be used for comparing the trends for all parameters. A p value of <0.05 will be conducted significant.

Null Hypothesis Ho

There is a significant effect of medication on TB patients for thinning of RNFL thickness

Alternative Hypothesis H1

There is no significant effect of medication on TB patients for thinning of RNFL thickness

We have adopted One sample mean test by using 'z' test.

$$Z = (\bar{x} - \mu_0) / (\sigma / \sqrt{n})$$

$\bar{x}$ is the sample mean

μ_0 is the standard RNFL thickness

σ is the standard deviation

n is the sample size

DISCUSSION

$Z=1.96$ (This is our critical value at 5% level of significance)

According to our all calculated z value mentioned, all = 0.05 are greater than the critical value of z.

Therefore, we are rejecting our null hypothesis and highly significant p value support our alternative hypothesis. From this statistical significance result, our study can infer that there is no possibility of RNFL thinning in TB patients taking ethambutol for short period of time.

CONCLUSION

We displayed that patient receiving TB medications, which were the basic medicines of anti-tubercular treatment, didn't experienced thinning in RNFL after the treatment period. This study could be attributed to factors such as a relatively small sample size limiting statistical power, unique characteristics or exposures in the study population, differences in measurement and classification methods, inadequate control for confounding variables, varying levels of risk factor exposure, failure to account for potential interactions or effect modifications, and examining associations at a single time point rather than over a longitudinal period. These methodological and population-specific differences may have contributed to the contrasting findings compared to other studies that reported positive associations between patients taking TB medications and RNFL thinning.

No significant associations were found between TB medications and RNFL thinning.

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