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Ophthalomology

A PROSPECTIVE STUDY OF OCULAR TOXICITY IN PATIENTS RECEIVING ETHAMBUTOL IN A TERTIARY HEALTH CARE HOSPITAL IN KOLKATA, EASTERN INDIA.

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ABSTRACT **BACKGROUND:**India accounts highest burden of tuberculosis cases about 2.64millions with incidence of 193 in year 2019(WHO). India is among the largest countries to implement National Tuberculosis Elimination Program(previously known as RNTCP). This program provides now daily regimen to the patients,where patients have to take daily dosage of ethambutol according to the body weight category of patients along with others ATDs ,which is a cause of concern,particular with regard to the ocular toxicity of ethambutol.The present study was undertaken to explore the ocular toxicity in the newly diagnosed cases of tuberculosis patients registered under the program in terms of visual acuity,color vision,optic disc findings,visual field and IOP changes. **AIMS AND OBJECTIVES**:Early detection of ocular changes due to ethambutol toxicity and early stoppage of ethambutol from the further ocular damages. STUDY DESIGNS:Hospital based prospective observational study for approximately one year(April 2020 to March 2021) in a tertiary health care centre in Kolkata. **METHODS:**Both eyes of 53 newly diagnosed tuberculosis patients were examined prior to start ATDs(including ethambutol),four and eight weeks after initiation phases and anytime within eight weeks in case of sudden onset of ocular complaints.Visual acuity,color vision,optic disc findings,field of vision,IOP were noted,tabulated and analyzed. **RESULTS:** Out of 106 eyes in 53 patients, decrease in visual acuity was seen in 10eyes(9.43%) ,impairment in red-green color in 12eyes(11.32%),optic disc abnormalities in 6eyes(5.66%) and visual field changes were seen in 8eyes(7.55%).The defects were bilateral in all cases.There were no significant changes in IOP within 8weeks commencement of ethambutol therapy.The patients with ocular changes were advised to stop ethambutol and showed significant improvement in vision on follow up later. **CONCLUSION:**In our study populations of 53 patients, 6patients (11.32%)were found with ocular changes due to ethambutol toxicity. So early detection of ocular changes due to ethambutol toxicity has great importance for its prevention.So baseline ophthalmological examination prior to start ethambutol and periodic follow up can prevent untoward irreversible vision loss due to ethambutol toxicity.

KEYWORDS : Ethambutol,tuberculosis,ocular toxicity,ocular changes

INTRODUCTION:

India is among the countries that carry the highest burden for tuberculosis, and accounts 2.64 millions of tuberculosis cases with incidence of 119 in year 2019(WHO). To combat this gigantic problem the National Tuberculosis Elimination Program (previously known as RNTCP) has been implemented throughout the country. Under this program patients receive fixed dose combination of ATDs daily under supervision. The safety and efficacy of the regimens have been well-documented, but there are still concerns regarding the ocular toxicity of ethambutol, because of its dose(15mg/kg/day). Ethambutol is a bacteriostatic drug, developed in 1961. Since then, mild-to-severe toxic amblyopia due to ethambutol has been reported by several authors.[1-3] Toxic optic neuritis may be of early or late onset, may be reversible or irreversible, and axial or peri-axial[4-5]. Ethambutol can cause visual impairment as a result of retrobulbar neuritis, which is related to the dose and duration of treatment. There are several controversial reports in medical literature regarding the safety of ethambutol and fear of its use as a routine anti-tubercular drug, especially in children. Due to the paucity of medical literature regarding the dose and duration related incidence and clinical manifestations of ethambutol induced ocular toxicity, this study was conducted by early detection of ocular changes and by early stoppage of ethambutol under the program.

METHODOLOGY

It is a prospective observational study of one year duration from April 2020 to March 2021 in the Ophthalmology department of RG Kar Medical College and Hospital.Both eyes of 53 newly diagnosed tuberculosis patients were examined prior to start ATDs,four and eight weeks after initiation phases and any time within eight weeks in case of sudden ocular complaints.Visual acuity,color vision,optic disc findings,field of vision,IOP were examined in this regards.

Baseline visual acuity was considered from 6/6(log MAR 0.0)[log minimum angle of resolution] to 6/60(log MAR 1.0).Visual acuity loss was counted if patient exceeded two Snellen chart lines between two successive follow up in the absence of other causal factors. Best corrected visual acuity was considered prior to start ethambutol in all cases.Color vision was recorded with full series of 14 Ishihara color vision plates and color vision impairment was considered if patients read atleast 9 or fewer plates correctly.Atleast Amsler grid was used to detect central field of vision abnormality in every patient prior to start ethambutol and periodic follow up along with Humphrey field analyzer for central and peripheral field .Any constrictions in visual field centrally or peripherally or both in follow up period and its absence prior to start ethambutol was considered as significant.Newly developed optic disc edema and temporal pallor in follow up period were counted as optic disc abnormalities due to ethambutol toxicity.IOP between 10-21mm of Hg considered as normal.

RESULTS

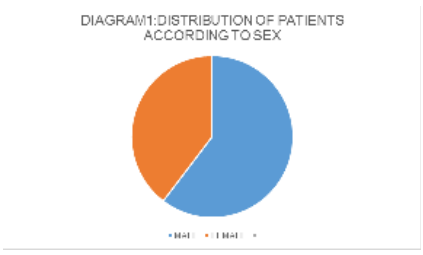
We started the study with 70 newly diagnosed tuberculosis patients after their consents but 53 patients were able to prescribed follow up and constituted the study group.

There were 32 males and 21 females in our study group between age 8yrs to 70 yrs with a mean age 40.396±15.184yrs. Out of 106 eyes in 53 patients, decrease in visual acuity was seen in 10eyes(9.43%).The mean of baseline visual acuity was 0 .094±0.121 prior to start ethambutol and mean 0.224±0.236 after 8weeks commencement of ethambutol with a $p<0.01$,which is highly significant. Impairment in red-green color was seen in 12eyes(11.32%).Optic disc abnormalities in 6eyes(5.66%) with disc edema in 2eyes and temporal pallor in 4eyes. Visual field changes were seen in 8eyes(7.55%) with central defect in 2eyes,peripheral defect in 4eyes and both in 2eyes.The defects were bilateral in all cases.There were no significant changes in IOP within 8weeks commencement of ethambutol therapy.The patients with ocular changes were advised to stop ethambutol and showed significant improvement in vision on follow up later.

TABLE 1. DISTRIBUTION OF PATIENTS ACCORDING TO SEX

MALE	FEMALE	TOTAL
32(60.37%)	21(39.63%)	53(100%)

TABLE 2. DISTRIBUTION OF PATIENTS ACCORDING TO AGE-SEX CATEGORY



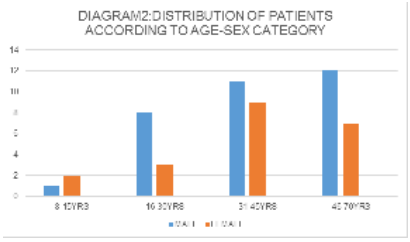
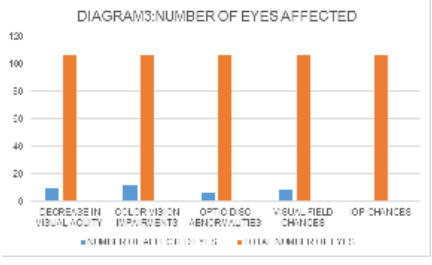


TABLE 3. NUMBER OF EYES AFFECTED(OUT OF 106 EYES IN 53 PATIENTS)

OPHTHALMOLOGICAL EXAMINATION	DECREASE IN VISUAL ACUITY	COLOR VISION IMPAIRMENTS	OPTIC DISC ABNORMALITIES	VISUAL FIELD CHANGES	IOP CHANGES
AT 4 WEEKS	4	4	2	0	0
AT 8WEEKS	4	6	4	6	0
ANYTIME WITHIN 8 WEEKS IN CASE OF SUDDEN OCULAR COMPLAINTS	2	2	0	2	0
TOTAL EYES	10(9.43%)	12(11.32 %)	6(5.66 %)	8(7.55%)	0



DISCUSSION:

Ethambutol is being used as ATDs since 1960 and recognition of ocular toxicity of ethambutol was first reported by Carr and Henkind in 1962[6].The incidence of toxicity is variably reported in the literature at the presently using dose of 15mg/kg/day.In our study none of the patients developed clinical symptoms as reported in a prospective study done by Menon et al[7] except subclinical toxicity as changes in visual acuity ,color vision,optic disc,field of vision.

According to Polak et al.[8] color vision disturbances are probably the most sensitive indicator of early ethambutol optic neuropathy which can occur even before visual acuity ,visual field changes.Our study also support it.

Various studies showed there may be visual field defects in form of central,peripheral or both which also revealed in our study.In general visual field defects occurs with the use of higher dosages of the drug especially in cases with obvious visual deficits.[9,10]

There are no clear risk factors for irreversible visual damages due to the drug but old age,renal insufficiency,chronic smoking are said to increase toxicity[7].None of these were found in our study population. In the present study patients recieved ethambutol 15mg/kg/day.Krishnaswamy[11] and mittal et al.[12] did not find any retrobulbar neuritis which support our study while Roy et al.[13]and Sharma et al.[14] found 3% toxicity in cases of using dosage of ethambutol 25mg/kg/day.

Study by Kandel et al.[15]revealed a statistically significant change in the visual acuity,as was found in our study.

The limitation of this study could be the ocular toxicity contributed by isoniazid,as revealed by Sahin et al.[16],which was not taken under consideration.

CONCLUSION:

In our study population of 53 patients, 6 patients(11.32%) were found with ocular changes due to ethambutol toxicty.So early detection of ocular changes due to ethambutol toxicity has great importance for its prevention. So baseline ophthalmological examination prior to start ethambutol and periodic follow up can prevent untoward irreversible vision loss due to ethambutol toxicity.Patient should be educated about blurring of vision,problems in appreciating different colors and non seeing area of central field while taking ethambutol as it is important to preseve sight while treating tuberculosis.

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