Visual Loss following Daily Dose Regimen of Anti Tubercular Treatment

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Abstract
This article is to report on the increasing trend of visual loss following daily regimen of Anti Tubercular treatment. Review of 15 patients who presented with varying degrees of visual loss after starting Anti Tubercular treatment was done. The patients had variable time of presentation ranging from few weeks to 3 months. Pupillary reaction was bilaterally brisk but ill sustained in 80% cases. Fundus examination showed optic disc changes only in 20% cases. Ethambutol was stopped in all cases. 46.6% patients were given systemic steroids. Patients who presented early had better visual prognosis. No treatment was found to be effective in reversing the optic neuropathy except stopping of Ethambutol. Only early diagnosis could prevent total visual loss. Till the time the causes and risk factors get better elucidated it would be prudent to have a regular Ophthalmological evaluation of all patients who are started on daily regimen of anti-tubercular treatment.

Methods
This study is a retrospective chart review of 15 patients who developed visual loss after treatment with the daily regimen of Anti Tubercular Treatment (ATT) for a period ranging from 1 month to 1 year. They presented to the outpatient department of Ophthalmology of Government Medical College, Kozhikode, Kerala, India between January 2018 to June 2019. Details regarding the age, gender, duration of ATT taken, comorbidities, renal status, smoking or alcohol dependence, time when the visual symptoms were noticed after starting ATT were noted. Clinical features included visual acuity, anterior segment findings, pupillary reaction, color vision, visual field, fundus findings at presentation and in last follow up, visually evoked potential (VEP), treatment given, fundus picture and visual acuity at last follow up and the time period that the patient has been on follow up were noted. Only those patients whose visual symptoms developed after the initiation of daily regimen of ATT and in whom the symptoms could be attributed to the Anti tubercular treatment and had been on follow up for at least 6 months were included in the study.

Results
Demographic Characteristics- The age of the patients ranged from 34 to 75 years. 8 (53%) patients were male and 7 (46.6%) patients were female. All patients presented with diminution of vision bilaterally which started after 1 month to 9 months of starting daily regimen of ATT treatment. They presented to the hospital within 15 days to 3 months of onset of symptoms. 5 patients (33%) had received ATT for pulmonary tuberculosis, 7 (46.6%) patients for Potts spine, 1 (6%) patient for laryngeal tuberculosis, 1 (6%) patient for intestinal tuberculosis and 1 patient (6%) for lupus vulgaris. 7 (46.6%) patients had associated diabetes mellitus and hypertension, 1 (6%) patient had peripheral vascular disease, 1 (6%) patient had a seizure disorder, 1(6%) patient had a...
history of cerebrovascular accident and 1 (6%) patient had a chronic kidney disease. All diabetic patients had a normal renal profile. Only 3 (20%) patients had a history of smoking and alcohol consumption for many years.

### Clinical features

**Visual acuity**- 7 (46.6%) patients had a profound loss of vision in both eyes i.e. VA <3/60. 3 (20%) patients had bilateral severe visual impairment (3/60 – 6/60). 4 patients (26.6%) had asymmetric presentation with one eye having profound vision loss and the other with a vision ranging from 6/60 to 6/18. 1 patient (6%) presented with visual acuity of 6/9 and 6/18 in RE and LE respectively with no further improvement. 6 (85.7%) patients out of 7 with profound loss of vision had presented late for ophthalmological evaluation at around 3 months. Rest of the patients presented between 2 weeks to less than 3 months. 1 patient with bilateral severe visual impairment did not reveal her history of ATT intake till 3 months even though she remained on continuous follow up for her diabetic retinopathy.

Anterior segment was unremarkable in all patients except 2 (13.3%) who had nuclear sclerosis grade 2. Pupillary reaction was bilaterally brisk but ill sustained in 12 (80%) patients. 3 patients (20%) had Grade 1 relative afferent pupillary defect (RAPD) in the more severely affected eye while the other eye showed a sluggish pupillary reaction. Color vision tested using Ishihara’s color plates, was defective bilaterally in 11 (73.3%) patients while in 3 (20%) patients it could not be tested due to profound loss of vision. In 1 (6%) patient there was a loss of color vision in only the severely affected eye.

Field examination showed a hemianopic field defect in 1 (6%) patient with profound loss of vision. Rest of the patients with profound loss of vision the field examination was not possible. Field examination showed central scotoma and centrocaecal scotoma (Figure 1) with peripheral field constriction in 9 (30%) eyes of 7 patients with bilateral severe visual impairment and patients with asymmetric loss of vision. 1 (6%) patient had a minimal loss of vision did not have any visual field defect.

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12 eyes of 7 patients (40%) had minimal optic disc pallor at the time of presentation, 6 (20%) eyes of 4 patients had optic disc edema and 12 (40%) eyes of 7 patients had normal optic disc at presentation. 1 (6%) patient with normal optic disc had a macular scar bilaterally at the time of presentation and had a history of poor vision since young age. 1 (6%) had moderate non proliferative diabetic retinopathy with non-center involving macular edema in both eyes.

**VEP** was done in 10 (66.6%) patients and it showed an absence of waves bilaterally in 8 patients (80%) and low amplitude with prolonged latency in BE of 2 patients (22%).

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**Table 1:** Master Chart showing the details of the 15 patients who developed visual loss following daily dose regimen of ATT

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**Figure 1:** Central & Centrocaecal Scotoma in a patient with Asymmetric visual loss due to Ethambutol induced optic neuropathy
Magnetic resonance imaging of the brain was carried out in 3 patients (20%) which showed small vessel disease in 2 patients and an old infarct in the midbrain in 1 patient. Demographic and clinical features are further described in Table 1.

Treatment

All patients were advised to stop Ethambutol with immediate effect after consultation with their RNTCP physician. 2 (13.3%) patients with profound loss of vision who did not show any improvement even after stopping Ethambutol for 1-2 weeks were advised to stop Isoniazid. 7 patients (46.6%) were started on systemic steroid: 2 patients (13.3%) were given pulse therapy of methyl prednisolone 1 gram intravenously for 3 days and then oral steroids on tapering schedule. 2 patients (13.3%) were given injectable steroids 2cc intravenously twice a day for 5 days and then gradually tapered and 3 patients (20%) were given oral steroids 40-60 mg twice daily for 5 days then tapered over a week. All were given methylcobalamine and multi vitamin tablets. At the last follow up at 6 months, 6 (20%) eyes of 4 patients with optic disc edema went into secondary optic atrophy. 10 (33.3%) eyes of 6 patients with normal optic disc continued to have a similar fundus picture at last follow up at 6 months. 2 eyes (6%) of a single patient with normal disc at presentation developed temporal disc pallor. 12 (40%) eyes of 7 patients had persistent or worsened temporal pallor at the time of last follow up.

Only 8 (26.6%) eyes of 4 patients showed any improvement of vision. 2 eyes of single patient with profound loss of vision bilaterally showed an objective improvement in vision from no perception of light (No PL) to 6/12 in BE. 4 eyes of 2 patients with bilateral severe visual impairment showed improvement from 3/60 in RE and 5/60 in LE to 6/60 and 6/36 in RE and LE respectively in 6 months. One patient with asymmetric visual loss showed improvement in vision from 6/60 to 6/12 in right eye and while in left eye there was only a marginal improvement from CFCF to 2/60.

6 (20%) eyes of 3 patients showed deterioration of vision even after stopping ethambutol. 14 (46.6%) eyes of 7 patients showed stabilization of vision after stopping Ethambutol.

Discussion

Ethambutol induced optic neuropathy is a well-recognized adverse effect which is dose and duration related. Prompt recognition of symptoms of diminution of vision could help in drastically reversing the optic neuropathy in 6.6% patients and marginally reversing it in 20% patients but rest of the patients did not show any improvement. The studies in the past have shown variability in the percentages of patients regaining their vision after stopping Ethambutol. This variability could be due to the difference in the follow up period of these patients apart from many known and unknown factors.

The patients who recovered their vision came within 2 weeks to 1 month of their onset of visual symptoms. All patients who reported late after their visual symptoms started did not benefit by stopping of Ethambutol. 13.3% of patients were also advised to stop Isoniazid when stopping of Ethambutol was not found to be effective after 2-3 weeks.

These patients did not show any improvement but further loss of vision could be prevented.

In the patients who recovered their visual acuity 50% patients had no comorbidities while 50% were diabetic with normal renal functions. 6% patients had chronic kidney disease and did not recover any vision even after cessation of Ethambutol. Renal disease has been a known risk factor for development of optic neuropathy following ATT. There were 46.6% diabetic patients and hypertensive patients all of whom had normal renal profile at the time of presentation and during follow up too. Patients with altered renal status require more frequent follow up with their ophthalmologists as the risk of Ethambutol induced optic neuropathy is found to be more in patients with reduced glomerular filtration rate since ethambutol is mainly excreted through kidney.

None of these patients who recovered their vision had any history of smoking or alcohol consumption. Only 20% of patients in this group had history of smoking and alcohol intake. All of them maintained their visual acuity following stoppage of Ethambutol.

Conclusions

Adverse drug reactions to ATT has seen an increase following the daily regimen of Anti Tubercular treatment. This calls
for a more rigid regimen of ophthalmological evaluation and follow up for all patients who are started on this new regimen. This would help in early detection of drug induced optic neuropathy and other adverse drug reactions which may help in saving the vision of the patient before irreversible damage has happened. This article is a small step in this direction to create awareness among all ophthalmologists regarding this drug induced optic neuropathy following daily regimen of anti-tubercular treatment.

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