A Revised Algorithm for Screening for Ethambutol-Associated Optic Neuropathy

Louie JK[1], Padmanabhan SP[2], Agraz-Lara R[1], Huang M[1], Min-Maing K[1], Cheng E[1], Lee G[1], Miller T[1], Keh, C[1]

1. San Francisco Department of Public Health (SFDPH) Tuberculosis Prevention and Control Program
2. Zuckerberg San Francisco General Hospital (ZSFG) -University of California San Francisco Department of Ophthalmology

Background

Ethambutol-associated optic neuropathy (EAON) reportedly occurs in <2% of persons on tuberculosis treatment (cumulative incidence 19.2/1000) (1, 2). Higher prevalence of EAON (6%) has been reported in patients on long-term (mean 16.1 months) ethambutol treatment for *Mycobacterium avium* disease (3). Onset can be sudden, with loss of visual acuity (VA) and red-green color discrimination, central scotomas and decreased peripheral fields. Risk factors include older age, impaired creatinine clearance, high dose (>27.5 mg/kg) or prolonged duration of ethambutol (range 2-9 months), hypertension and human immunodeficiency virus infection (4). Permanent and irreversible EAON (visual impairment ≥3 months) has been rarely observed. Current recommendations include baseline and monthly VA and color discrimination exams in patients on ethambutol, and monthly assessment for new visual disturbances (4). However, assessing VA can be challenging in certain populations, including those who have baseline visual deficits, dementia, or are homebound.

The SFDPH Tuberculosis Clinic provides care for all San Francisco residents diagnosed with active tuberculosis; in 2017, 107 cases were treated. Ethambutol is part of the standard initial treatment regimen. Routine screening for EAON has traditionally included monthly testing for VA (Snellen test) and red-green color discrimination, with referral for ophthalmologic evaluation for decreased VA identified on screening exam or new visual complaints.

Objectives

We implemented a new screening algorithm in order to identify EAON as early as possible.

Methods

In October 2017, in-service training on VA assessment, including Ishihara testing, was provided to clinic staff by ophthalmology experts. Clinic staff were educated on the importance of routine monthly visual acuity exams and monthly assessment of patients for any new visual disturbances, as well as reviewing dosing to ensure that ethambutol was dosed at <20 mg/kg range.

Additionally, all patients meeting the following criteria were referred for formal ophthalmologic evaluation: 1) age ≥ 60 years, creatinine clearance ≤ 60 ml/min and on ethambutol for > 3 months OR 2) baseline decrease VA with no prior workup OR 3) noted difficulty complying with routine VA screening in clinic. Patients on ethambutol >6 months were referred for monthly ophthalmologic screening. All patients on ethambutol were counseled to call immediately if they experienced concerning visual symptoms.

Results

During 6 months (November 7, 2017-April 7, 2018) of implementation of the new algorithm, 25 patients meeting the above criteria were referred for ophthalmologic screening. Of these, four cases of EAON were confirmed by ophthalmologic exam (Table); ethambutol was discontinued immediately. The average duration of ethambutol treatment was 289 days (9.6 months). All cases recovered except one, who continued to have progressive worsening visual acuity 11 weeks after stopping ethambutol and 5 weeks after stopping all tuberculosis medications (Figure).

	Age (yrs)	Medical Co-morbidities	CrCl	EMB dose mg/kg	EMB total days	How EAON initially suspected	Symptoms	Snellen and Ishihara
Patient #1	64	DM, HTN, renal transplant 2004	66	16.3	224	Symptoms	Blurry vision left>right	Decreased VA, 1/12 color plates
Patient #2	87	Dementia, Rheumatoid arthritis	34	16.5	315	Routine ophthalmology screening	No visual complaints	Normal Snellen and Ishihara
Patient #3	72	None	54	17.2	323	Symptoms	Blurry vision. Unable to watch TV or read.	Abnormal, loss of VA from baseline, red-green discrimination normal
Patient #4	78	Dementia, COPD, esophagitis, FTT	75	19.5	294	Routine ophthalmology screening	No visual complaints	Not performed due to patient inability to comply

Abbreviations: yrs- years, CrCl-creatinine clearance, EMB-ethambutol, EAON-ethambutol associated optic neuropathy, DM-diabetes mellitus, HTN-hypertension, VA- visual acuity, COPD-chronic obstructive pulmonary disease, FTT- failure to thrive

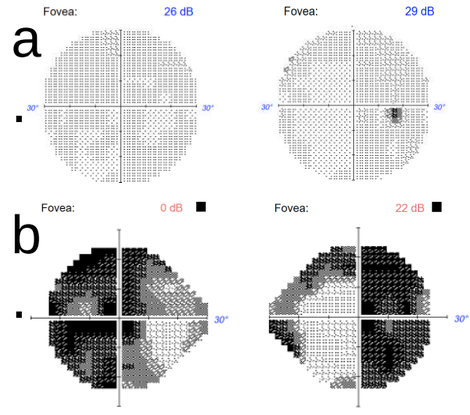

Figure (Patient #1):

(a) Humphrey Visual Field 30-2 grayscale plot and already subnormal foveal thresholds, right and left eye respectively, at the time of initial diagnosis. Darker areas indicate visual field defects.

(b) Humphrey Visual Field 24-2 grayscale plot and diminished foveal thresholds, right and left eye respectively, 9 weeks later. Note progression despite discontinuation of EMB.

Conclusions

Using an aggressive screening algorithm, we identified four new cases of EAON in a 6 month period. Two were asymptomatic and might otherwise have been missed. EAON may be underdiagnosed with current screening recommendations, particularly in the elderly or demented patients or those who are homebound. TB providers should be trained in routine assessment for EAON and patients should be routinely educated on the signs and symptoms of EAON. Referring asymptomatic high–risk patients for routine ophthalmologic evaluation may help early diagnosis and cessation of ethambutol, possibly averting complications and permanent visual loss due to EAON.

References

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Contact: Janice Louie at Janice.louie@sfdph.org