A Revised Algorithm for Screening for Ethambutol-Associated Optic Neuropathy

Louie JK1, Padmanabhan SP2, Agraz-Lara R3, Huang M1, Min-Maing K1, Cheng E3, Lee G1, Miller T1, Keh, C1

1. San Francisco Department of Public Health (SFDPH) Tuberculosis Prevention and Control Program
2. Zuckerberg San Francisco General Hospital (ZSFHG)-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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (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 and new visual complaints (4). However, assessing VA can be challenging in certain populations, including those who have baseline visual deficits, dementia, or are homebound.

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.

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).

Results

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.

Conclusions

Acknowledgements: Thank you to all clinic staff who are involved in providing patient care and support. Special thanks to Dr. Gisela Schechter for her never-ending willingness to provide expertise and insights on our most challenging cases.

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

References


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.

Abbreviations: yrs, years; EM: ethambutol; CrCl EMB: ethambutol creatinine clearance; DM: diabetes mellitus; HTN: hypertension; VA: visual acuity; COPD: chronic obstructive pulmonary disease; FTT: failure to thrive; CrCl, creatinine clearance.