Training HIV clinicians in eye examination to diagnose cytomegalovirus retinitis

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Abstract

Problem Acquired immunodeficiency syndrome (AIDS)-related cytomegalovirus (CMV) retinitis continues to be a neglected source of blindness in resource-poor settings. The main issue is lack of capacity to diagnose CMV retinitis in the clinical setting where patients receive care and all other opportunistic infections are diagnosed.

Approach We developed and implemented a four-day workshop to train clinicians working in human immunodeficiency virus (HIV) clinics how to perform binocular indirect ophthalmoscopy and diagnose CMV retinitis. Workshops comprised both classroom didactic instruction and direct clinical eye examinations in patients with advanced AIDS. Between 2007 and 2013, 14 workshops were conducted in China, Myanmar and the Russian Federation.

Local setting Workshops were held with local clinicians at HIV clinics supported by nongovernmental organizations, public-sector municipal hospitals and provincial infectious disease referral hospitals. Each setting had limited or no access to locally-trained ophthalmologists, and an HIV-infected population with advanced disease.

Relevant changes Clinicians learnt how to do binocular indirect ophthalmoscopy and to diagnose CMV retinitis. One year after the workshop, 32/38 trainees in Myanmar did systematic eye examination for early diagnosis of CMV retinitis as standard care for at-risk patients. In China and the Russian Federation, the success rates were lower, with 10/15 and 3/5 trainees, respectively, providing follow-up data.

Lessons learnt Skills necessary for screening and diagnosis of CMV retinitis can be taught in a four-day task-oriented training workshop. Successful implementation depends on institutional support, ongoing training and technical support. The next challenge is to scale up this approach in other countries.
Introduction

Acquired immunodeficiency syndrome (AIDS)-related cytomegalovirus (CMV) retinitis is a potentially blinding opportunistic infection that used to occur in up to one-third of HIV-infected patients in high-income countries before the availability of antiretroviral therapy (ART). It accounts for over 90% of the blindness related to human immunodeficiency virus (HIV) infection.\(^1\) CMV retinitis has virtually disappeared in high-income countries due to the routine early diagnosis of HIV infection and initiation of ART. Now, CMV retinitis primarily affects HIV-infected patients in middle and low-income countries who are diagnosed with advanced immunodeficiency (late presenters) in settings with limited resources or poor access to care.\(^2,3\)

The fundamentals of CMV retinitis management are early diagnosis, specific anti-CMV treatment and ART.\(^4\) Diagnosis is achieved by clinical examination; the gold standard is binocular indirect ophthalmoscopy through a dilated pupil, performed by a trained examiner.\(^3\) Early diagnosis requires systematic screening of all patients with CD4+ T lymphocyte counts less than 100 cells/\(\mu\)L, because retinal damage may already be irreversible and extensive by the time the patient first reports symptoms.\(^5\) Unfortunately, ophthalmological care is generally not available to HIV patients in resource-poor settings because of stigma associated with the disease and the logistical challenges of referring patients who are gravely ill. Ophthalmologists are often not available at all, or are not motivated or trained to treat HIV-related eye complications. Since ophthalmologists are traditionally the only clinicians trained in both indirect ophthalmoscopy and diagnosis of CMV retinitis, timely ophthalmic consultation for diagnosis of CMV retinitis in resource-poor settings is virtually never achieved.\(^6\)

In a wide selection of settings, we have directly observed the lack of diagnostic capacity, absence of systematic screening of high-risk patients, and dire clinical consequences of delayed diagnosis of CMV retinitis.\(^3\) A growing body of evidence demonstrates poor clinical outcomes in CMV retinitis, with 21–36% of eyes already blind when the patient is first examined by an ophthalmologist.\(^3,7\) An increasing number of patients are successfully being treated for HIV, yet left permanently blind,\(^8\) and there has been no apparent decrease in the burden of CMV retinitis over the past decade.\(^2\)

Approach

During a 2006 evaluation of AIDS-related eye complications conducted by an ophthalmologist in HIV clinics in Myanmar, the high prevalence and consequences of failure to diagnose CMV
retinitis became apparent. Therefore, a short, goal-oriented workshop in collaboration with other clinicians and ophthalmologists was devised for training non-ophthalmologist HIV clinicians to perform indirect ophthalmoscopy and diagnose CMV retinitis. This workshop was supported by the SEVA Foundation, Médecins Sans Frontières, Medical Action Myanmar and other nongovernmental organizations (NGOs). The workshop model evolved and improved over the course of 14 iterations in China, Myanmar and the Russian Federation; the current version is described in Box 1.

Workshop success is based on three key factors. First, the technique of indirect ophthalmoscopy is divided into small, well-described steps, accompanied by intensive practice with model eyes, and supported by four days of individual attention from trainers. Second, the didactic material is highly repetitive and the curriculum has a narrow focus on material necessary for diagnosis of serious AIDS-related opportunistic infections of the eye: CMV retinitis, HIV retinopathy, choroidal tuberculosis, syphilis, necrotizing herpetic infection, toxoplasmosis and myelinated nerve fibre layer. This narrow focus is logical and appropriate, given the extremely high pretest probability that any white lesion diagnosed by indirect ophthalmoscopy in a patient with advanced AIDS will be either CMV retinitis or a cotton-wool spot. The curriculum is not designed for training clinicians in primary eye care. Third, the workshop is based on active individual and group participation, and immediate immersion in clinical care. Trainees, both novice and experienced, participate in the didactic programme by presenting most lectures, and they spend over half their time examining and diagnosing patients. Experiential learning begins with clinical examinations on the first day and provides immediate context for future didactic material.

Relevant changes
To evaluate the implementation of CMV retinitis screening programmes following the workshops, we contacted former trainees and their supervisors to review self-reported clinical performance in the first year after training. We trained 65 people over the 14 workshops, of these, 58 were expected to provide clinical screening for CMV retinitis (two trainees failed to demonstrate satisfactory qualifications, and five were HIV advisors or administrators taking the course for educational purposes). We received information either from the trainee or a supervisor for 53 of the 58 (91.4%) successful trainees. Of these 53 trainees, 46 (86.8%) performed CMV retinitis screening in the first year after the training. During this year, a median of 120 screening
examinations (interquartile range, IQR: 61–300) were performed and a median of 15 (IQR: 6–40) cases of CMV retinitis were diagnosed per trainee (Table 1).

Workshops have been conducted in Myanmar since 2007. This has directly led to systematic screening for CMV retinitis in HIV clinics for the majority of patients at risk enrolled in HIV treatment nationally. Screening coverage extends over most of the country, including areas in conflict. At the end of 2013, 67,643 patients were under treatment with ART in Myanmar, with 37,500 (55%) of these patients enrolled in the NGO programmes that provide routine screening for CMV retinitis. This success has occurred within the institutional structure of well-supported NGO programmes, with highly motivated clinicians, and with ongoing training and technical support.

In China, despite difficult communication and the almost complete lack of opportunity to provide technical support after the workshop, there was apparent evidence of success. Most trainees (10/11) provided information that they have implemented eye examination in their clinical care and are diagnosing cases of CMV retinitis. We had limited opportunity to guide trainee selection before the workshops, and several trainees were either unsuited to implementing retinal screening in their setting, did not work regularly in an HIV clinic or subsequently left the country to study overseas.

There was initial success in the Russian Federation. However, it was not sustained, due to trained clinicians being transferred, political difficulties in providing technical support, ambiguous health-care policies regarding eye skills for HIV clinicians and weak institutional support.

Discussion
Although this initiative is not part of current World Health Organization policy, we believe that examination of the retina by indirect ophthalmoscopy should be part of the standard initial physical examination for all HIV-infected patients who first present with advanced immunodeficiency. About 35% of individuals infected with HIV in low-income countries have a CD4+ T lymphocyte count less than 100 cells/µL before starting ART treatment; these are patients at risk for CMV retinitis. Our experience, gathered over more than a decade, supports the strategy of clinicians diagnosing and treating CMV retinitis at the primary care level, as they currently diagnose and treat all other major opportunistic infections. We found that HIV
clinicians in all three settings were generally motivated and enthusiastic to learn eye examination skills, and could be trained to accurately diagnose CMV retinitis. Furthermore, we found that clinicians completing the workshop had good agreement with expert ophthalmologists regarding the diagnosis of CMV retinitis.\textsuperscript{13} This is consistent with a recent systematic review that found no difference in the reported prevalence of CMV retinitis, whether screening was performed by an ophthalmologist or by an HIV clinician trained in retinal examination.\textsuperscript{2}

Once diagnosis of CMV retinitis is achieved, timely and appropriate anti-CMV treatment can be provided. The issue of treatment is not covered in this report, except to note that both intravitreal injection of ganciclovir and oral treatment with valganciclovir can be provided by trained clinicians at the primary care level.\textsuperscript{13,14}

Routine point-of-care eye examination for HIV late presenters provides ancillary benefits. There is evidence that indirect ophthalmoscopy can immediately identify some patients with disseminated tuberculosis if choroidal tubercles are seen, allowing for earlier diagnosis and treatment.\textsuperscript{15} Finally, cotton-wool spots, strongly associated with high HIV viral load,\textsuperscript{16} may be clinically helpful for monitoring response to ART in settings without access to viral load testing, identifying patients who are non-adherent or who have a drug-resistant strain of HIV.

In conclusion, one of the main lessons learnt (Box 2) is that a well-designed four-day workshop is feasible and effective for training clinicians to perform indirect ophthalmoscopy and diagnose CMV retinitis. Clinical impact depends on the institutional support provided by the health-care system, and sustained training and technical support. To scale up these workshops, we need to provide widely accessible didactic materials; develop methods to systematically monitor clinical performance, and offer mentorship in the months following the workshop (e.g. via telemedicine); and identify clinicians who are willing and able to be future trainers. If these challenges can be met, we believe the fundamental necessary innovation of transferring ophthalmic skills and primary management of CMV retinitis to the HIV clinician will reduce the prevalence of AIDS-related blindness in middle- and low-income countries.

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Competing interests:
None declared.

References


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<tr>
<td>No of trainees</td>
<td></td>
<td></td>
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<tr>
<td>Enrolled in workshop</td>
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<td>Satisfactory completed workshop</td>
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<tr>
<td>Were expected to perform screening(^a)</td>
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<td>38</td>
<td>5</td>
</tr>
<tr>
<td>Have follow-up data available</td>
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<td>38</td>
<td>3</td>
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<tr>
<td>Performed screening during first year</td>
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<td>32</td>
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<td>HIV patients screened, median (IQR(^b))</td>
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<td>230.5 (100–430)</td>
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<td>Patients diagnosed with CMV retinitis, median (IQR)</td>
<td>6.5 (5–20)</td>
<td>20 (9.5–47.5)</td>
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CMV: cytomegalovirus; HIV: human immunodeficiency virus; IQR: interquartile range.

\(^a\) Advisors and administrators occasionally completed the workshop; these individuals were not expected to perform screening.

\(^b\) Of those who performed screening, self-reported by each trainee or a supervisor.
BOX 1 Workshop description

Between three and six HIV/AIDS clinicians are enrolled for each workshop. Trainees are selected based on interest in learning eye examination skills, high motivation, at least one year of HIV clinical experience, an ongoing position in a clinical HIV programme where their skills will be needed and practised, and ideally younger than 30 years. The lead ophthalmologist and trainer is trained in uveitis and experienced in AIDS-related eye disease; one or two other ophthalmologists commonly provide teaching support. During the workshop each trainee has exclusive use of a portable battery-powered indirect ophthalmoscope (ScanOptics, Adelaide, model SO-2200), a 28D lens, and a homemade model eye. One month before the workshop, the series of lectures comprising the workshop curriculum is emailed to each trainee for independent study.

The first morning comprises six short lectures on ocular anatomy, basic bedside examination of the eye and binocular indirect ophthalmoscopy, followed by practice with model eyes. The second and third mornings comprise a series of lectures on CMV retinitis and the differential diagnosis of AIDS-related retinal disease. The initial six lectures are presented to the group by the trainees. Mornings begin with discussion of problems and written tests on prior material. The final morning begins with a written examination based on retinal photographs, emphasizes common patient management scenarios, and is followed by lengthy discussion. Throughout the workshop, whenever time is available, the trainers lead teaching sessions based on photographic examples of pathology. Each afternoon (3–5 hours) trainees examine dilated eyes of patients either known to have CMV retinitis or at high-risk of AIDS-related retinal disease. A typical workshop has five patients the first day and 10 on each of the following three days. Trainees examine and make retinal drawings of both eyes of every patient. During the first 1–2 days, trainees bring their model eye with them to the bedside and go back and forth from model eye to patient whenever they encounter technical difficulty. Trainees review lecture material each evening and are required to spend at least 30 minutes practising indirect ophthalmoscopy with model eyes during the first two evenings. There are final written course evaluations by each trainee, and by the lead trainer, for consideration in improving the next workshop.
**BOX 2 Summary of main lessons learnt**

- A four-day training workshop can teach the skills of indirect ophthalmoscopy and diagnosis of CMV retinitis to motivated clinicians who can then successfully screen patients for AIDS-related CMV retinitis at the primary care level.

- One year after the workshop most of the trainees were providing systematic eye examination for early diagnosis of CMV retinitis as standard care for at-risk patients.

- Successful implementation depends on institutional support, ongoing training and technical support.