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Research Paper

Ebola Virus Persistence in Ocular Tissues and Fluids (EVICT) Study: Reverse Transcription-Polymerase Chain Reaction and Cataract Surgery Outcomes of Ebola Survivors in Sierra Leone☆

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ABSTRACT

Background: Ebola virus disease (EVD) survivors are at risk for uveitis during convalescence. Vision loss has been observed following uveitis due to cataracts. Since Ebola virus (EBOV) may persist in the ocular fluid of EVD survivors for an unknown duration, there are questions about the safety and feasibility of vision restorative cataract surgery in EVD survivors.

Methods: We conducted a cross-sectional study of EVD survivors anticipating cataract surgery and patients with active uveitis to evaluate EBOV RNA persistence in ocular fluid, as well as vision outcomes post cataract surgery. Patients with aqueous humor that tested negative for EBOV RNA were eligible to proceed with manual small incision cataract surgery (MSICS).

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Findings: We screened 137 EVD survivors from June 2016 – August 2017 for enrolment. We enrolled 50 EVD survivors; 46 with visually significant cataract, 1 with a subluxated lens, 2 with active uveitis and 1 with a blind painful eye due to uveitis. The median age was 24.0 years (IQR 17–35) and 35 patients (70%) were female. The median logMAR visual acuity (VA) was 3.0 (Snellen VA Hand motions; Interquartile Range, IQR: 1.2-3.0, Snellen VA 20/320 – Hand motions). All patients tested negative for EBOV RNA by RT-PCR in aqueous humor/vitreous fluid and conjunctiva at a median of 19 months (IQR 18-20) from EVD diagnosis in Phase 1 of ocular fluid sampling and 34 months (IQR 32-36) from EVD diagnosis in Phase 2 of ocular fluid sampling. Thirty-four patients underwent MSICS, with a preoperative median VA improvement from hand motions to 20/30 at three-month postoperative follow-up ($P < 0.001$).
Interpretation: EBOV persistence by RT-PCR was not identified in ocular fluid or conjunctivae of fifty EVD survivors with ocular disease. Cataract surgery can be performed safely with vision restorative outcomes in patients who test negative for EBOV RNA in ocular fluid specimens. These findings impact the thousands of West African EVD survivors at-risk for ocular complications who may also require eye surgery during EVD convalescence.

1. Introduction

Uveitis syndromes due to ocular viral infection can lead to significant visual morbidity and blindness (Connors et al., 2015). In addition to commonly recognized pathogens (e.g. herpes simplex virus, cytomegalovirus), emerging viruses (e.g. chikungunya, zika) are increasingly implicated as causes of uveitis (Connors et al., 2015). The West African Ebola virus disease (EVD) outbreak in 2013–2016 brought attention to a range of uveitis findings ranging from anterior uveitis to sight-threatening panuveitis as a sequelae of Ebola virus infection diagnosed in 13% to 34% of EVD survivors (Varkey et al., 2015; Tiffany et al., 2016; Shantha et al., 2017; Hereth-Hebert et al., 2017). A complex disease spectrum was noted, leading to severe vision impairment or blindness in nearly 40% of affected eyes (Shantha et al., 2017). Vision loss due to uveitis impacts overall quality-of-life amidst a number of other clinical sequelae of EVD, including arthralgias, myalgias, headache, and abdominal pain (Epstein et al., 2015; Vetter et al., 2016).

Ebola virus (EBOV) has been noted to persist in immune privileged sites including the aqueous humor (Varkey et al., 2015) and cerebrospinal fluid (Jacobs et al., 2016), leading to severe uveitis and meningoencephalitis, respectively, during EVD convalescence. Long-term EBOV RNA detection in semen (Deen et al., 2017; Soka et al., 2016), breast milk (Sissoko et al., 2017), and placenta (Bower et al., 2016), with rare transmission events reported (Sissoko et al., 2017; Bower et al., 2016; Mate et al., 2015; Diallo et al., 2016), highlight the individual and public health consequences of EBOV persistence and emphasize the urgent need to investigate EBOV RNA clearance from immune-privileged sites.

In EVD survivors, invasive ophthalmic procedures (e.g. cataract surgery, open globe repair, retinal detachment surgery) currently pose an uncertain risk of EBOV transmission via ocular fluid to health care workers and close contacts of EVD survivors. We conducted The **E**bola **Vi**rus Persistence in O**c**ular **T**issues and Fluids (EVICT) study to establish an evidence base for a safe, effective approach to invasive ophthalmic procedures in EVD survivors. Anterior chamber paracentesis was performed in patients with active uveitis or in patients who require ophthalmic surgery to test for EBOV viral persistence before intraocular surgery. Herein, we report the clinical ophthalmic phenotypes, prevalence of EBOV RT-PCR in ocular fluid of a cohort of Sierra Leonean EVD survivors anticipating ocular surgery or with active uveitis. We also describe the vision restorative outcomes of patients meeting criteria for cataract surgery.

2. Methods

We designed a cross-sectional study to evaluate EBOV RNA persistence in ocular fluids and tissues of EVD survivors. Institutional Review Board approval was obtained from Emory University and the Office of Ethics and Scientific Review Committee, Sierra Leone Ministry of Health and Sanitation (MOHS). Human research was conducted according to the Tenets of the Declaration of Helsinki, and informed consent was obtained with the assistance of Sierra Leonean interpreters in the native dialect of enrolled patients. During the ocular fluid sampling portion of the EVICT Study, patients underwent ocular fluid testing for EBOV RNA by RT-PCR. Patients who tested negative for EBOV RNA were then eligible for the surgical portion of the EVICT Study, which included manual small-incision cataract surgery (MSICS) with intraocular lens (IOL) implantation when medically indicated.

2.1. EVICT Facility, Study Site Preparation, and Personal Protective Equipment

Patient ophthalmologic evaluations were conducted at the Lowell and Ruth Gess Eye Hospital in Freetown, Sierra Leone. An ophthalmic procedure room was designed adhering to World Health Organization (WHO) guidelines (World Health Organisation, 2016), and guidance from the Emory University Serious Communicable Disease Unit (SCDU), with high-level safety precautions for potential EBOV exposure (Fig. 1). Eye care providers performed the ocular fluid sampling procedure in full personal protective equipment (PPE) with monitoring from an infectious disease physician trained in the care of EVD in the acute Ebola treatment unit (ETU) setting.

2.2. Patient Recruitment

EVD survivors anticipating ophthalmic surgery (cataract and/or retinal surgery) were identified via an ophthalmic screening program conducted by the MOHS National Eye Care Program from March 2015 through March 2016. In addition, EVD survivors were referred from local eye clinics for vision loss and cataract evaluation. These centers included Connaught Government Hospital (Freetown), Lunsar Baptist Eye Hospital (Port Loko) and Kenema Government Hospital (Kenema), as well as direct referral from the Sierra Leone Association of Ebola Survivors (SLAES).

2.3. Patient Screening, Ophthalmic Exam, and Follow-Up

Ophthalmic exams for EVD survivors included corrected visual acuity (VA), pupillary examination, confrontational visual fields, ocular motility and intraocular pressure (tonopen, Avia, Reichert Technologies). Anterior chamber (AC) cell grade was measured per Standardization of Uveitis Nomenclature guidelines via slit lamp examination (Jabs et al., 2005). Cataract was classified as nuclear sclerotic, posterior subcapsular, anterior subcapsular, uveitic white cataract, uveitic white cataract with anterior capsular fibrosis, and graded from one to four. Funduscopic evaluation was performed with a 90- and 28-diopter