Remote Home Monitoring of Early-to-Intermediate Age-Related Macular Degeneration

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OBJECTIVE Describe patients with non-exudative age-related macular degeneration (AMD) in a home monitoring program through Kaiser Permanente Southern California's (KPSC) eye monitoring program (EMP).

PURPOSE KPSC's AMD EMP was established to provide a home monitoring solution for AMD patients. This program aims to provide earlier detection of visual changes in patients. EMP heightens the patient's awareness of their condition through empowering their ability to effectively monitor at home. This leads to earlier detection which is the key to preservation of vision.

METHODS Patients with early to intermediate AMD are enrolled into the EMP by ophthalmologists or optometrists. Upon enrollment, patients are tracked in our database and reminded to do home monitoring with an Amsler grid using our telephone reminder system or our web based mobile app. Patients that are reminded electronically are shown an Amsler grid on their device. OCT and VA are checked once a year. Only patients with Amsler grid, OCT or VA changes are referred for further evaluation. Otherwise, the patients are monitored and followed with an ophthalmic exam only every 3-4 years. A retrospective review of the first 100 patients was done.

RESULTS The first 100 patients with at least 1 year follow-up were analyzed. There were 62% female, 73% White, 14% Hispanic, 8% Asian, 3% Black and 2% Other with an average age of 74.4 (SD 10.7). Median visual acuity at baseline was 20/25 OD and 20/25 OS. Median visual acuity at year 1 was 20/25 OD and 20/30 OS. Mean baseline central foveal thickness was 276.3 (37.2) OD and 273.1 (31.5) OS. Mean year 1 central foveal thickness was 282.1 (46.0) OD and 276.2.1 (36.2) OS. Average number of optom/ophtho visits for non-EMP AMD patients vs. EMP AMD patients were 2.4 (3.1) versus 1.0 (1.4). Patients were also surveyed and over 90% said the program was extremely/very helpful and would recommend it to others.

CONCLUSION KPSC's AMD EMP provides a high quality solution that enhances home detection of visual changes. By minimizing routine visits to the physician, it is cost-effective and convenient to the patient. In addition, the program increases patient awareness of their condition to better detect earlier changes in AMD, leading to timely treatment and better overall treatment outcomes.

TAKE HOME MESSAGE Home monitoring increases opportunity for non-exudative AMD patients to self-detect early visual changes, leading to improved care quality and patient convenience.

Detection of Asymptomatic Neovascularization in Intermediate Age-Related Macular Degeneration Using Swept Source Optical Coherence Tomography Angiography

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OBJECTIVE Identification of asymptomatic subclinical type 1 macular neovascularization in eyes with intermediate age-related macular degeneration (iAMD) using swept source optical coherence tomography angiography (SS-OCTA).

PURPOSE To identify asymptomatic subclinical type 1 macular neovascularization in eyes with intermediate age-related macular degeneration (iAMD) using swept source optical coherence tomography angiography (SS-OCTA).

METHODS SS-OCTA was performed as part of a prospective IRB–approved study at the Bascom Palmer Eye Institute. Consecutive patients with iAMD in one eye and neovascular AMD in their fellow eye were imaged. Some of these patients also underwent fluorescein angiography (FA) and indocyanine green angiography (ICGA). Images from these three angiographic techniques were compared when available. The incidence of subclinical type 1 neovascularization in asymptomatic eyes with

intermediate age-related macular degeneration (iAMD) was assessed based on SS-OCTA imaging.

RESULTS Fifty-nine consecutive patients with iAMD in one eye and neovascular AMD in their fellow eye were imaged with SS-OCTA between August 2014 and January 2016. Clinical examination of the 59 eyes with iAMD revealed drusen and pigmentary abnormalities in the central macula and no evidence of macular fluid on routine OCT imaging. SS-OCTA revealed unambiguous type 1 macular neovascularization in 10 of the 59 eyes. In the 11 eyes with concomitant angiographic imaging, macular plaques were observed in three eyes, and SS-OCTA identified type 1 macular neovascularization in all three eyes. Five of the 10 eyes with subclinical CNV had at least 4 months of follow-up (range 4 to 11 months) and none of these eyes became symptomatic.

CONCLUSION SS-OCTA is a fast, non-invasive, detailed, depth-resolved imaging strategy for the identification of non-exudative neovascular lesions in eyes with iAMD. In our population, the incidence of these asymptomatic lesions was 17%. Due to the risk of exudative transformation, we recommend close follow-up of these eyes, but we do not recommend treating these eyes with anti-VEGF therapy until more is known about the natural history of these lesions.

TAKE HOME MESSAGE SS-OCTA can identify choroidal neovascularization in eyes with intermediate AMD before macular fluid appears and before patients become symptomatic from the exudation.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Nucleoside Analogs and Derivatives as Therapies for AMD

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OBJECTIVE To determine whether nucleoside reverse transcriptase inhibitors (NRTIs), i.e. nucleoside analogs, are beneficial in age-related macular degeneration (AMD)

PURPOSE We showed that nucleoside analogs inhibit the inflammasome and can be repurposed for dry and wet AMD (Fowler et al. *Science* 2014; Mizutani et al. *IOVS* 2015). To determine whether patients using NRTIs are protected against development of AMD, and to test whether modified NRTIs, which block inflammasome but lack the toxicity of NRTIs associated with RT inhibition, are effective in models of AMD.

METHODS Retrospective cohort study of patients aged 55 years or older with HIV or Hepatitis B and no preexisting record of AMD in a large US managed care network from January 1, 2001, through December 31, 2014. Three NRTIs (d4T, AZT, and 3TC), as well as their methoxy-modified derivatives, were administered intravitreously or intraperitoneally in multiple mouse models of RPE degeneration (*Alu* RNA, oligomerized amyloid beta peptide, iron, complement anaphylatoxins, sodium iodate, or paraquat) and CNV (laser injury). RPE damage was imaged using fundus and histological imaging at 1 week. CNV volume was quantified by confocal imaging at 1 week.

RESULTS Of 3,753 patients with viral infections, 373 (9.9%) developed AMD. Incident AMD among NRTI users (5.7%) was significantly less than that among patients who never used NRTIs (10.6%) (P = 0.0004, two tailed chi squared test). For each year of NRTI use, the risk of developing AMD was decreased by 18% (hazard ratio=0.82; 95% CI, 0.70-0.97; P=0.02, Cox regression). In all mouse models tested, all the NRTIs and their derivatives completely blocked RPE degeneration, and reduced CNV volume by 30-60%.

CONCLUSION NRTI use is associated with reduction in risk of developing AMD in this patient population. Other anti-viral medications did not confer a similar AMD risk reduction. Nucleoside analogs and modified derivatives were effective in numerous animal models of RPE degeneration and CNV. If confirmed by prospective clinical trials, these findings could lead to novel treatments for dry and wet AMD.

TAKE HOME MESSAGE NRTIs usage in patients is associated with reduced incident development of AMD. NRTIs and modified NRTIs protect against pathology in numerous animal models of dry and wet AMD.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Severe Vision Loss After Intravitreal Injections of Autologous Adipose Tissue-Derived Stem Cells for Age-Related Macular Degeneration

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OBJECTIVE To report on severe vision loss after intravitreal injections of autologous adipose tissue-derived stem cells for dry age-related macular degeneration in three patients.

PURPOSE To report three patients with severe vision loss after bilateral intravitreal injection of autologous adipose tissue-derived stem cells for non-neovascular age-related macular degeneration. All three patients were seen following participation in a patient funded research study conducted at the same stem cell clinic.

METHODS This is a consecutive case series. Presenting visual acuity (VA), surgical management, and visual acuity outcomes are reported.

RESULTS Three patients developed severe vision loss after bilateral intravitreal injections of autologous adipose tissue-derived stem cells. The last documented best-corrected VA (BCVA) prior to injection ranged from 20/40 to 20/200. Presenting VA after the experimental procedures ranged from counting fingers to light perception (LP). All patients had severe vision loss associated with ocular hypertension, hemorrhagic

retinopathy, vitreous hemorrhage, combined traction/rhegmatogenous retinal detachment, and/or lens dislocation. After three months, the VA ranged from 20/400 to LP.

CONCLUSION Intravitreal injection of autologous adipose tissue-derived stem cells can result in poor vision.

TAKE HOME MESSAGE Intravitreal injection of autologous adipose tissue-derived stem cells performed at stem cell clinics can result in poor visual outcomes.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval