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Original Article

Preferential Hyperacuity Home Testing for Monitoring Intermediate Age-related Macular Degeneration in Routine Clinical Practice

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ABSTRACT

Objectives: A home monitoring device (ForeseeHome; Notal Vision, Tel Aviv, Israel) detected choroidal neovascularization in age-related macular degeneration (AMD) earlier than home and office monitoring. This study describes device usage in routine clinical practice.

Materials and Methods: An Institutional Review Board-approved retrospective chart review of intermediate AMD patients who used the device at a single tertiary care center. Primary outcomes were duration and frequency of usage and outcomes of alerts generated.

Results: Sixty-two patients (106 eyes) completed monitoring 4.2 ± 2.1 times per week (avg ± std dev) from February 2015 to February 2019. Forty-five eyes discontinued monitoring after an average of 65 days (range 13–237 days), due to poor quality tests (62%), and false-positive alerts (16%). Eyes that discontinued device monitoring were older and had poorer visual acuity than eyes that continued monitoring ($P < 0.01$). Fourteen alerts were generated, of which one represented conversion to exudative AMD. Two additional converted eyes were identified by routine office visit and Amsler grid monitoring.

Conclusions: Home monitoring has the potential to improve the detection of exudative AMD. Identifying barriers to device utilization are necessary in the AMD population.

Keywords: Age-related macular degeneration, ForeseeHome, Preferential hyperacuity testing

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of blindness among adults age 50 or greater worldwide, with the exudative form of AMD accounting for 90% of vision loss.[1,2] In the US, the prevalence of exudative AMD is estimated at 1.8 per 1000 white Americans age 50 and up. The US Census Bureau estimates that by 2050, the population older than 65 will double and the oldest population, age greater than 85, will increase from 5.1 million in 2010 to 2019 million in 2050, which represents a significant increased number of patients with AMD.[3,4] Worldwide, it is projected that approximately 288 million people will suffer from AMD by 2040.[5]

Treatment of choroidal neovascular (CNV) membranes in exudative AMD can preserve or improve vision, but visual outcomes depend on early detection and treatment of CNV membrane.[6] The best predictor of visual outcomes at 1- and 2-years is visual acuity at treatment

initiation; worse baseline visual acuity is associated with poor vision at 5 years.[7,8] At present, conversion to exudative AMD is detected by a combination of symptom monitoring, Amsler grid use, and routine office exam. However, the Amsler grid is less sensitive to visual changes when compared to other methods of monitoring such as perimetry, fundus exam, or retinal imaging.[9,10] Patients may not detect changes, or they are unable to adhere to the recommended daily self-monitoring. Fine and associates reported that despite self-reported regular Amsler grid use, a majority of patients with CNV and vision loss only noticed new changes when presented with an Amsler grid in the office.[11]

A preferential hyperacuity perimetry-based home monitoring device (ForeseeHome, Notal Vision, Tel Aviv, Israel) was developed to improve monitoring of AMD progression in the central 14° of vision.[12] The device presents an artificial distortion to a patient, who is then asked to identify location of the distortion. Approximately 500 data points are tested between 3 and 5 times over a 3-min test period. Test results of each eye are transmitted to the device company and compared to the patient's baseline measurements and a normative database. Alerts are sent to the prescribing provider if a significant change in testing is found. The Home Monitoring of the Eye Study (HOME study) compared the home monitoring device and standard care with standard care alone in 1520 participants at risk of developing exudative AMD.[12] Standard care consisted of investigator specific instructions for home monitor which may include Amsler grid use. Eyes in the device arm had better vision at time of CNV diagnosis than eyes receiving standard care, with 87% of eyes monitored with the device having 20/40 vision or better versus 62% of eyes in standard care alone. Fifty-one percent of CNV detected in the device group were detected using the device alone, before symptom development. The number of eyes with CNV detected at a scheduled office visit was reduced from 45.2% in the standard group to 27.4% in the device group. Importantly, subjects' usage data were transmitted and if it dropped below a certain threshold, they would be contacted by the monitoring center to troubleshoot the cause or remind the patient to use the device. Cases where the device detected new conversion to neovascular AMD have also been reported in the literature.[13]

While studies have shown the benefit of device monitoring compared to Amsler grid, there have been few reports on using the device in routine clinical practice, which lacks the frequency of reminders to use the device or support to troubleshoot problems. The un-masked study population in the HOME study was also subject to selection and patient bias. The purpose of this study was to characterize usage patterns and to determine the feasibility of the home monitoring device in routine clinical practice and in a real world setting.

MATERIALS AND METHODS

This was a retrospective chart review of patients who used the home monitoring device at the Cole Eye Institute of the Cleveland Clinic (Cleveland, Ohio) between February 15, 2015, and February 5, 2019. Institutional Review Board approval was obtained. Inclusion criteria included a diagnosis of intermediate AMD (either bilateral large drusen [2 study eyes], or large drusen in 1 eye [study eye] with advanced AMD in the fellow eye), and best corrected visual acuity of better than 20/60 verified by the physician at the time of ordering. Fellow eyes being treated with anti-VEGF injections less than every 3 months were included in the study. Exclusion criteria included retinal pathology including diabetic retinopathy, center involving visual field defects such as due to severe glaucoma, and geographic atrophy.

The primary outcome was duration and frequency of device use. Secondary outcomes included the frequency of true- and false-positive alert(s) and number of additional office visits created in response to alert(s). Reasons for device discontinuation were also tabulated. Baseline characteristics and outcomes were descriptively described. Continuous variables were described using mean and standard deviation. Categorical variables were described using frequency and percentages. Comparison between groups was performed using Students's *t*-test or non-parametric Mann–Whitney U, assuming significance at $P < 0.05$. This study was not powered for comparative outcomes.

RESULTS

A total of 124 patients were prescribed use of the monitoring device by their personal ophthalmologist. Sixty-five patients registered data with the ForeseeHome device from February 15, 2015, to February 5, 2019, and were included in the study [Figure 1]. One patient started device monitoring in February 2015; the remainder obtained the device after summer of 2017. Three patients were excluded because only one instance of device use was registered during the study period for unknown reasons. Overall, data were collected for 324 days following the start of device monitoring. On *post hoc* analysis of 62 patients, there were 23 patients (12 females and 13 males) who were termed "former" device users and had discontinued the device for at least 14 days before study end-date. There were 39 "current" device users (12 females and 19 males) were deemed to be actively using the device based on registered device data within 2 weeks of end-date. The groups were compared to determine if there were characteristics associated with ability to use the device regularly during study period. The mean age at time of device prescription was 76.9 ± 6.8 years of age. The mean age was older among former device users (79.8 ± 6.4 years) when compared to current device users (75.3 ± 6.4 years, P = 0.006).

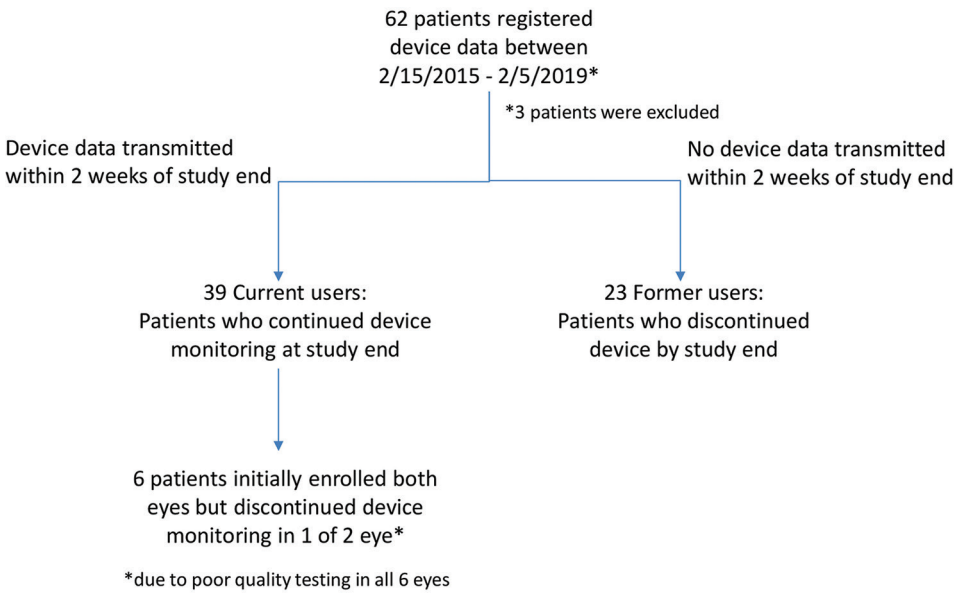

Figure 1: Device use among patients who registered device data. Sixty-two patients from Cole Eye Institute registered device data between February 15, 2015, and February 5, 2019. At the end of this study, 39 of the 62 patients were considered current users who had actively transmitted data with the preceding 2 weeks. Of the current user group, six had initially enrolled bilateral eyes; however, monitoring was discontinued in one of two eyes due to poor quality testing. Twenty-three of the 62 patients were considered former users with no device data being transmitted within the preceding 2 weeks.

Of 62 included patients, 44 enrolled bilateral eyes and 18 enrolled one eye. Advanced macular degeneration that was not being actively treated (15 patients) was the most common cause of unilateral eye enrollment, followed by non-arteritic ischemic optic neuropathy (1), vitreomacular traction (1), and unknown (1). This resulted in a total of 106 eyes with intermediate AMD (61 current, and 45 former) monitored for an average of 160.1 days (range 13–1446). Baseline visual acuity was 0.11 ± 0.11 logMar (approximate Snellen ~20/26) among all eyes enrolled. Former eyes that discontinued monitoring had an average of 0.17 ± 0.14 logMar acuity (Snellen ~20/30) at baseline, compared to 0.07 ± 0.07 (Snellen ~20/23) in current eyes that continued monitoring ($P < 0.001$).

Overall, the mean duration of device use was 160 days (range 130–1446 days) among the 106 eyes that registered device data. There was an average of 4.2 ± 2.1 tests completed each week. The 61 current eyes registered an average use of 3.6 ± 1.6 times/week over 230 days (range 13–1446 days). The 45 former eyes registered an average of 4.9 ± 2.3 times/week over 65 days (range 13–237 days), including eight eyes that were monitored more than 7 times per week.

There were 14 alerts generated in 14 eyes of 11 patients. Office visits were arranged for all alerts. One patient cancelled the alert-generated office visit and was found to have stable dry AMD disease at the routine visit 6 months later. One patient was evaluated at an outside facility without unknown outcome but continued device use. Of the remaining 12 alerts, office visits were completed a median of 5 days after alert generation (range 1–9 days). Eleven alerts represented false positives with patients having stable disease as determined by OCT and/or fluorescein angiography. One alert represented conversion to exudative AMD in an asymptomatic patient and anti-VEGF treatment was initiated. The baseline acuity was 20/30, and the acuity at CNV detection was 20/40. There were two additional eyes converted to exudative AMD and did not trigger a device alert. One was detected on routine office visit (baseline acuity 20/25, and 20/50 at detection) and one was detected by home Amsler monitoring (baseline acuity 20/30, and 20/30 at detection). All three patients (four eyes) discontinued device use after conversion to exudative AMD.

Time to device discontinuation is described in [Figure 2]. Causes for device discontinuation in 45 eyes included poor quality tests (28/45 eyes) as determined by the device company, false-positive alerts (7/45 eyes), and unknown reasons (5/45 eyes). Monitoring in four eyes was discontinued following conversion to exudative AMD, and monitoring in one eye was discontinued due to interval development of a central retinal vein occlusion.

DISCUSSION

A chart review of patients with non-exudative AMD who were prescribed use of the home monitoring device to

detect progression to exudative AMD was performed. Of 124 patients who were prescribed use of the device, 106 eyes of 61 patients underwent device monitoring.

A significant portion (49%) of patients who were recommended the device did not proceed to use it. The reason why a patient decided to forego device monitoring was not recorded in the medical record and not obtainable within the limits of a retrospective chart review. Limited notes in the medical record included financial burden of the device, technologic barriers to device use, and disinterest in device monitoring. Further study into barrier to device use is necessary to fully reach the potential of device monitoring described in the HOME study.

Of the 61 patients who obtained the device, 23 patient discontinued device use during the follow-up period. This was much more frequent than in the HOME study where 109/763 (14%) discontinued the device. Patients in our study used the device less frequently than in the HOME study (4.4 ± 1.7 times/week over a mean of 1.4 years). Among participants that continued to use the device in the HOME study, only 57/609 (9.4%) patients tested eyes less than twice weekly. In contrast, 6/39 (15.4%) patients who continued using the device in our group used the device less than twice weekly. Over time, frequency of device use declined in our study [Figure 3]. Nonetheless, after an average of 230 days, the patients who continued to use the device completed at least three tests per week, on average, which demonstrates the feasibility of regular device monitoring.

Differences in patient selection, qualification testing, and technical support contributed. Our cohort was recruited from routine office patients, who are not representative of the observed research study population. Unlike the HOME study, where qualification tests excluded 20% of potential participants due to pre-existing visual field defects and a further 8% of participants due to unreliable responses, no qualification testing was performed in-office before obtaining the monitoring device. The most common cause for device discontinuation (unreliable testing and inability to establish baseline) is also consistent with the previous studies, which found 15% of patients were unable to complete a tutorial and 8% had unreliable testing.[14] Visual acuity was also poorer in eyes that discontinued monitoring ($P < 0.001$). The older AMD population is also less facile with technology. Unlike the HOME study, there was less support to troubleshoot device difficulties and fewer reminders to encourage device use. To improve duration of ease of monitoring among the elderly, the device would benefit from more extensive qualification testing and user support.

Number of alerts (14) was also higher than the rate of 0.24 alerts/year reported in the HOME study. One alert reflected new CNV conversion, and 12 alerts were false-positive alerts that did not demonstrate evidence of CNV by either OCT or fluorescein angiography. A disproportionate number of alerts resulted from bilateral eyes of three patients, which suggested user difficulty contributed to alerts. Selection of the reliable patient and refinement of testing parameters may improve the positive predictive value of alerts in the routine office patient.

Routine exams and patient self-monitoring, in addition to home monitoring, were essential for early detection of CNV. Three patients out of 61 developed CNV membranes over

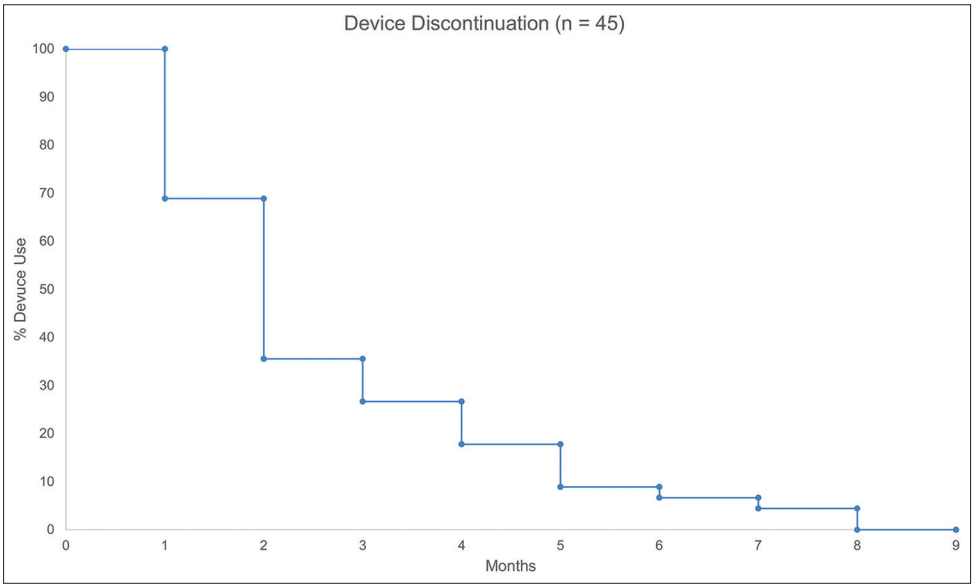

Figure 2: Time to device discontinuation. Survival curve demonstrating time to device discontinuation among patients who stopped device monitoring at time of study discontinuation ($n = 45$).

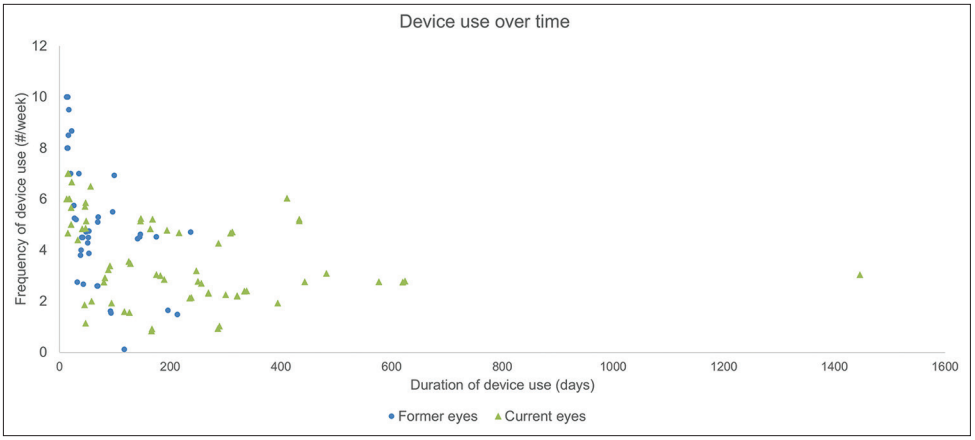

Figure 3: Frequency of device use over time. Frequency of device use is plotted against duration of device use for both formerly monitored eyes (discontinued device at study end) and currently monitored eyes (continued device at study end). The device was used most frequently within the 1st few months of initiation. Eyes monitored 200 days or more were able to maintain at least once a week testing.

324 days of follow-up following device use. One asymptomatic patient was detected by home monitoring, one based on Amsler grid use, and one in routine office exam. Visual acuity declined by two lines in the patient whose CNV was detected on routine exam, but was within one line of baseline in the two other patients. All were initiated on anti-VEGF therapy.

Multiple studies have shown that hyperacuity perimetry is more sensitivity to macular pathology[15-17] than Amsler grid, which has a variable sensitivity for CNV of 34–100%.[15,18] The sensitivity of the device in this cohort was 33.3% and specificity was 87.3%. In addition to the high rate of false-positive alerts, rate of conversion to neovascular AMD was lower in our cohort than previously reported.

CONCLUSION

We performed a retrospective chart review of routine office patients with intermediate stage AMD who used a home monitoring device to detect CNV development. Patients who maintained device monitor were able to transmit data regularly for an average of 230 days. The device detected CNV in an asymptomatic patient and visual acuity had only decline by one line at time of treatment initiation. All patients who generated alerts were expediently scheduled office visits. Device was discontinued most frequently due to poor baseline or unreliable testing. Poor testing also contributed to false-positive alerts and alert-generated office visits. The device website describes candidates for device use as having 20/60 vision or better, cognitive, and physical ability to use the device, and no confounding issues. Few patients who were prescribed the device proceeded to obtain it. Further studies are required to determine the barriers to obtaining the device. Our results also suggest that additional qualification testing and technological support are necessary to identify patients who are reliable candidates to initiate device monitoring and to ensure maintained use of the device. Refining test parameters may decrease the high rate of false-positive alerts seen in the routine AMD patients. Office exam and screening with the Amsler grid should also complement use of the home monitoring device, as CNV was detected by both methods in our study.

Limitations to our study include the lack of consistent classification of AMD severity. The use of optical coherence tomography, fundus photos, or fluorescein angiography to determine AMD stage was up to the discretion of treating ophthalmologist. No data are available regarding why certain patients prescribed used of the device decided whether to initiate device monitoring or not. The small sample size and short follow-up time with low incidence of choroidal neovascularization precluded any conclusions about the ability of the device to detect CNV. In addition, patients were prescribed the device continuously throughout the time period studied, and the variable start time may confound which patients appeared to continue or discontinue the device. Data may also be incomplete on chart review and no cause for discontinuation was identified for five patients. Nonetheless, our study suggests that there is a role for device monitoring in combination with Amsler grid use and office-based monitoring to detect exudative AMD.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. Rishi P Singh is on the Editorial Board of the Journal. Dr. Sharma reports personal fees from Genentech and

Eyepoint Pharmaceuticals, outside the submitted work .Dr. Rachitskaya reports personal fees from Novartis, outside the submitted work.Dr. Srivastava reports personal fees from Carl Zeiss Meditec, personal fees from Santen Pharmaceuticals, personal fees from Gilead Sciences, personal fees from Optos, personal fees from Clearside Biomedical, personal fees from Valeant Pharmaceuticals, royalties from Bioptigen, royalties from Synergetics, outside the submitted work.Dr. Kaiser reports personal fees from Regeneron, personal fees from Bayer, personal fees from Novartis, personal fees from Carl Zeiss Meditec, outside the submitted work.Dr. Singh reports personal fees from Carl Zeiss Meditec, personal fees from Eyepoint Pharmaceuticals, personal fees from Novartis, personal fees from Genentech, personal fees from Roche, personal fees from Regeneron, personal fees from Bausch and Lomb, personal fees from Alcon, personal fees from Bayer, outside the submitted work.

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