Retinal Function determined by Flicker ERGs before and after Intravitreal Injection of Anti-VEGF Agents

Gaku Terauchi
Department of Ophthalmology, Teikyo University School of Medicine
Kei Shinoda (Shinodak@med.teikyo-u.ac.jp)
Department of Ophthalmology, Teikyo University School of Medicine
Hiroyuki Sakai
Department of Ophthalmology, Teikyo University School of Medicine
Makoto Kawashima
Department of Ophthalmology, Teikyo University School of Medicine
Soichi Matsumoto
Department of Ophthalmology, Teikyo University School of Medicine
Atsushi Mizota
Department of Ophthalmology, Teikyo University School of Medicine
Yozo Miyake
Aichi Medical University

Research Article

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Abstract

Background: To evaluate the retinal function before and after intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents in the injected and non-injected eyes.

Methods: Seventy-nine eyes of 79 patients that were treated by an intravitreal injection of an anti-VEGF agent for age-related macular degeneration (AMD), diabetic macular edema (DME), or retinal vein occlusion (RVO) with macular edema (ME) were studied. The RETeval® system was used to record 28 Hz flicker electroretinograms (ERGs) from both eyes before (phase 1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3). Patients were grouped by disease or by the injected agent and compared. The significance of the changes in the implicit times and amplitudes was determined by *t* tests.

Results: The amplitudes were not significantly different among the groups. The implicit times were significantly longer or tended to be longer at phase 2 and 3 compared to phase 1 for each disease and for each injected agent in the injected and non-injected eyes.

Conclusions: The results show that an intravitreal anti-VEGF injection will prolong the implicit times not only in the injected eye but also in the non-injected eye soon after the intravitreal injection.

Trial registration: All of the patients gave a written informed consent and the study was conducted in accordance with the tenets of Declaration of Helsinki and approved by the Ethics Committee of the Teikyo University School of Medicine (study ID number: 14-122).

Keywords: Aflibercept, age-related macular degeneration, electroretinogram, intravitreal injection, macular edema, ranibizumab, retinal vein occlusion, vascular endothelial growth factor.

Background

Intravitreal injections are used to deliver drugs and gases to the retina and choroid to treat various eye diseases. Since pegaptanib, an anti-vascular endothelial growth factor (anti-VEGF) aptamer, was first approved by the United States Food and Drug Administration (U.S. FDA) in 2004, a growing number of intravitreal injections are being performed every day. Ranibizumab, aflibercept, and bevacizumab are commonly used as anti-VEGF agents [1-10]. The anti-VEGF agents were original used to treat eyes with age-related macular degeneration (AMD)[1-4] but its use has expanded to diabetic macular edema (DME) [5-10], retinal vein occlusion (RVO) with macula edema (ME)[11-14], and other vascular-related retinal diseases. Several clinical trials have reported on their effectiveness [1-14]. In addition, the use of intravitreal injections of oculi plasmin [15] and steroids has increased, and intravitreal injections have become a relatively common procedure.

However, serious local side effects such as endophthalmitis, vascular occlusions, retinal tears, and rhegmatogenous retinal detachment can develop in the injected eyes [16-19], and also systemic

complications such as cerebral and myocardial infarctions have been reported [20]. These findings indicate that these agents can have systemic affects and attention needs to be paid to these complications.

The evaluations of the retinal function by electroretinography (ERG) can be performed not only by conventional ERG systems [21-23] but also by the new RETeval system, a handheld, portable ERG device [21,24,25]. Previous studies evaluating retinal function by ERGs focused only on the injected diseased eye, and an evaluation of the non-injected fellow eye after an intravitreal injection of anti-VEGF agents has not been reported. We believed that the RETeval system could be easily applied to the assessment of the function of the fellow eye even just after injection especially when contact lens electrodes are not used.

Thus, the purpose of this study was to evaluate the retinal function before and at <2 h and between 2 and 24 h after an intravitreal injection of different anti-VEGF agents. We determined changes in the retinal function of the injected eye and non-injected fellow eye.

Methods

Patients

All of the participants had undergone an intravitreal injection of an anti-VEGF agent at the Teikyo University Hospital in Tokyo, Japan from June 2014 to August 2015 and were prospectively studied. Seventy-nine eyes of 79 patients had received the intravitreal injection of an anti-VEGF agent for AMD, DME, or RVO with ME. The injected anti-VEGF agent was ranibizumab or aflibercept (Table 1). If the patients had been injected more than once within the study period, only the initial data were used. In patients who had been injected in both eyes during the study period, only the data collected after the first injection was included.

Methods

Recordings of flicker ERG was done to meet our aim of evaluating the retinal function before and after an intravitreal injection of the anti-VEGF agents in a prospective manner.

Flicker ERGs were elicited and recorded three times from both eyes with the RETeval® system (Mayo, Inazawa, Japan); the first recording was before the injection of an anti-VEGF agent (phase 1), the second was within 2 hours after the injection (phase 2), and the third was 2 to 24 hours after the injection (phase 3). Recordings were made under room light after mydriasis, and the flicker ERGs were picked-up by a sensor strip skin electrode affixed to the lower eyelid of both eyes. The strips included the active, reference, and ground electrodes.

A mini Ganzfeld dome was placed in front of the eye and a 3 cd·s/m^2 flash with 30 cd/m^2 background light (ISCEV standard) was delivered to elicit the responses. The patients were instructed to look at a fixation point within the dome, and the patient's fixation was monitored by an infrared camera (Figure 1). The implicit times and amplitudes of the flicker ERGs were automatically analyzed by the software integrated in the RETeval® system.

Intravitreal injections

The intravitreal injections were done under topical 4% xylocaine anesthesia. The conjunctival sac was disinfected by 10% povidone-iodine and 0.05% chlorhexidine gluconate, and a sterile lid speculum was used. After the ocular surface was prepared, aqueous humor was aspirated from the limbus with a 30-gauge needle. The ocular surface was disinfected again with 0.25% povidone-iodine solution, and then 0.05 ml of the anti-VEGF agent was injected into the vitreous through the pars plana with a 30-gauge needle. Antibiotics eye drops and ointment were applied and a sterile eyepatch was placed over the eye.

The patients were grouped and compared by the type of disease or by the type of anti-VEGF agent injected. For statistics, *t* tests were used to determine whether the changes in the implicit times and amplitudes among the groups were significant. A *P* value of $P<0.05$ was taken to be significant.

Results

We excluded cases that did not have a complete set of recordings during the three phases, and also those whose amplitudes were too small to be analyzed by the RETeval system. In the end, 79 cases were analyzed and 9 cases were excluded.

Demographics of all cases (Figures 2 and 3, Table 2)

The mean age of the patients was 68.9 ± 12.6 years, and they were made up of 44 men and 35 women. The mean ± standard deviation of the implicit time in the injected eye was 31.2 ± 3.18 at phase 1, 31.7 ± 3.06 at phase 2, and 32.2 ± 3.31 msec at phase 3, and that in the non-injected fellow eye was 30.5 ± 3.30 at phase 1, 31.1±3.18 at phase 2, and 31.3 ± 3.39 msec at phase 3. The differences in the implicit times between phase 1 and phase 2, and between phase 1 and phase 3 were significant in both the injected and non-injected fellow eyes.

The amplitudes in the injected eyes were 8.66 ± 5.72 μV at phase 1, 7.88 ± 6.07 μV at phase 2, and 9.46 ± 8.93 μV at phase 3, and that in the non-injected fellow eye was 9.41 ± 6.48 μV at phase 1, 9.15 ± 6.66 μV at phase 2, and 9.51 ± 6.19 μV at phase 3. The differences in the amplitudes between the two eyes were not significant at any phase.

Subgroup analysis by disease (Figure 2; Table 3)

Thirty-seven eyes of 37 patients had AMD (mean age 74.1 ± 8.58 years, 24 men and 13 women), 24 eyes of 24 patients had DME (mean age 59.9 ± 11.3 years, 14 men and 10 women), and 18 eyes of 18 patients had RVO with ME (mean age 70.1 ± 14.9 years, 6 men and 12 women).

In the AMD group,18 eyes were injected with ranibizumab and 19 eyes injected with aflibercept. The mean implicit time in the injected eye was 29.9 ± 1.75 msec at phase 1, 30.4 ± 1.64 msec at phase 2, and 30.8 ± 2.14 msec at phase 3, and that in the non-injected fellow eye was 29.5 ± 2.46 msec at phase 1, 30.4 ± 2.11 msec at phase 2, and 30.6 ± 2.35 msec at phase 3. Significant differences in the implicit times between phase 1 and phase 2, and between phase 1 and phase 3 were found in both the injected and non-injected eyes.

The mean amplitude in the injected eye was 8.99 ± 5.74 μV at phase 1, 8.12 ± 6.43 μV at phase 2, and 9.04 ± 6.34 μV at phase 3, and that in the non-injected fellow eye was 10.1 ± 7.16 μV at phase 1, 9.63 ± 7.27 μV at phase 2, and 9.81 ± 6.18 μV at phase 3. No significant difference was observed in the amplitudes for both eyes.

The DME group included 18 eyes injected with ranibizumab and 6 eyes injected with aflibercept. The mean implicit time in the injected eye was 33.6 ± 3.22 msec at phase 1, 34.2 ± 3.15 msec at phase 2, and 34.7 ± 3.09 msec at phase 3, and that in the non-injected fellow eye was 33.6 ± 3.10 msec at phase 1, 34.1 ± 3.10 msec at phase 2, and 34.3 ± 3.40 msec at phase 3. The difference in the implicit times between phase 1 and 3 was significant in the injected and non-injected fellow eyes. No significant difference was observed between phase 1 and 2 in the injected and non-injected fellow eyes.

The mean amplitudes in the injected eye was 7.95 ± 5.88 μV at phase 1, 7.05 ± 5.83 μV at phase 2, and 7.56 ± 5.88 uV at phase 3, and that in the non-injected fellow eye was 7.53 ± 5.13 μV at phase 1, 7.15 ± 5.47 μV at phase 2, and 7.81 ± 5.59 μV at phase 3. No significant difference was observed in the amplitudes for any of the comparisons for both eyes.

The RVO with ME group included 14 eyes injected with ranibizumab, 3 eyes injected with aflibercept, and 1 eye injected with bevacizumab. The mean implicit times of the injected eye was 30.7 ± 3.68 msec at phase 1, 31.3 ± 3.37 msec at phase 2, and 31.6 ± 3.79 msec at phase 3, and that of the non-injected fellow eyes was 28.4 ± 1.93 msec at phase 1, 28.6 ± 2.00 msec at phase 2, and 28.9 ± 2.30 msec at phase 3. Significant differences between phase 1 and phase 2, and between phase 1 and phase 3 were observed only in the injected eyes.

The mean amplitude in the injected eye was 8.94 ± 5.72 μV at phase 1, 8.50 ± 5.82 μV at phase 2, and 12.9 ± 14.7 μV at phase 3, and that in the non-injected fellow eye was 10.5 ± 6.43 μV at phase 1, 10.8 ±

6.47 μV at phase 2, and 11.2 ± 6.74 μV at phase 3. No significant differences were observed for any comparisons in both eyes.

Subgroup analysis for different injected agents (Figure 3, Table 4)

Fifty eyes of 50 patients were injected with ranibizumab, 28 eyes of 28 patients were injected with aflibercept, and one eye of one patient was injected with bevacizumab. The eyes injected with ranibizumab were compared to the eyes injected with aflibercept. The mean age of the ranibizumab group (22 men, 28 women) was 68.1 ± 13.5 years, and 18 eyes had AMD, 18 eyes had DME, and 14 eyes had RVO with ME. The mean implicit time in the injected eye was 31.6 ± 3.45 msec at phase 1, 32.0 ± 3.45 msec at phase 2, and 32.5 ± 3.57 msec at phase 3, and that of the non-injected fellow eye was 30.8 ± 3.24 msec at phase 1, 31.3 ± 3.51 msec at phase 2, and 31.5 ± 3.62 msec at phase 3. Significant differences between phase 1 and 2, and between phase1 and 3 were observed in both the injected and non-injected eyes.

The mean amplitude of the injected eye was 7.18 ± 5.34 μV at phase 1, 6.68 ± 5.60 μV at phase 2, and 8.21 ± 9.97 μV at phase 3, and that in the non-injected fellow eye was 8.21 ± 6.00 μV at phase 1, 7.32 ± 4.79 μV at phase 2, and 8.31 ± 5.54 μV at phase 3. No significant differences were found for any comparisons in both eyes.

The mean age of the aflibercept-injected group (21 men, 7 women) was 70.1 ± 11.0 years, and 19 eyes had AMD, 6 eyes had DME, and 3 eyes had RVO with ME. The mean implicit time in the injected eye was 30.9 ± 2.43 msec at phase 1, 31.4 ± 2.09 msec at phase 2, and 31,8 ± 2.55 msec at phase 3, and that of the non-injected fellow eyes was 30.2 ± 3.33 msec at phase 1, 31.0 ± 2.36 msec at phase 2, and 31.3 ± 2.85 msec at phase 3. Significant differences between phase 1 and 2 and between phase1 and 3 were observed in the injected eyes, and significant difference was observed only between phase1 and 3 in the non-injected eyes.

The mean amplitude in the injected eye was 11.5 ± 5.41 μV at phase 1, 10.0 ± 6.49 μV at phase 2, and 11.8 ± 6.45 μV at phase 3, and that in the non-injected fellow eyes was 11.7 ± 6.86 μV at phase 1, 12.5 ± 8.23 μV at phase 2, and 11.8 ± 6.80 μV at phase 3. No significant difference was observed in any comparisons in both eye.

None of the eyes had a serious complication during the course of this study.

Discussion

The amplitudes of the flicker ERGs were not significantly different at the different phases in both eyes and all the subgroups classified by the injected agent or the disease. This is consistent with previous studies [21-23]. However, this lack of significant differences in the amplitudes of the flicker ERGs may be due to the relatively large variations in the amplitudes of the flicker ERGs.

On the other hand, the implicit times were significantly longer at phase 2 and 3 than at the baseline (phase 1) for each disease and for each injected agent except for phase 2 of the DME group. This differs from the results of Yasuda et al who reported that the implicit times of the flicker ERGs of the injected eyes were significantly shortened from 32.2 ± 2.6 msec to 30.6 ± 2.2 msec at one month after an intravitreal injection of ranibizumab in eyes with a central RVO [21]. They also reported that the implicit times of the injected eyes were significantly longer than that of the non-injected fellow eyes before the injection of ranibizumab. However, they did not compare the implicit times of the non-injected fellow eyes before and after the injection of ranibizumab into the affected eye. Holm et al reported that the implicit time of the 30 Hz flicker full-field ERGs were significantly shorter at 4 weeks after the third monthly injection anti-VEGF agents in eyes with DME [22]. Gabriel et la reported that all components of the implicit times and the amplitudes of the full-field ERGs were not significantly different at 12 and 24 weeks after the intravitreal injection of ziv-aflibercept in eyes with diabetic retinopathy [23]. The major difference between these studies and our study is the time when the parameters of the ERGs were assessed, viz., our measurements were made within 24 h of the injection while the other studies made the measurements 4 to 12 weeks after the injection. It requires some time for any agents to exert their therapeutic effects such as on the visual acuity or the improvement of macula edema. In our study, we may have been able to detect the influence of the anti-VEGF agents on the retina at a very earlier phase rather than after the therapeutic effects of the agents had occurred. Januschowski et al reported that no significant reduction in the amplitudes of the a- and b-waves of the isolated perfused bovine retina with aflibercept was observed at the end of the washout, but there were significant reductions in those directly after an exposure to aflibercept [26]. Myers et al reported that the mean amplitude of b-wave was significantly reduced 8 weeks after the intravitreal injection of the different anti-VEGF agents in normal rabbits [27]. Although their research was on rabbits, the ERGs were recorded at different post-injection times, and they showed a reduction in the b-wave amplitude. Our results are consistent with their conclusions that the anti-VEGF agent affected the retinal function adversely.

Our result showed that no significant difference in the implicit times of the non-injected fellow eye with aflibercept at phase 2 in contrast to that with ranibizumab at phase 2. This may be related to the differences in the time required for the agent to reach the fellow eye. Avery et al reported that the serum concentration of ranibizumab peaked at 3 hours after the intravitreal injection and aflibercept peaked at 1 day after the intravitreal injection [28,29]. This difference in the peak times may support our results of a time lag between the two agents.

In the perioperative period, we must consider the influence of the intraocular conditions that were changed by the intravitreal injection. There is a possibility that the postoperative intraocular pressure (IOP) may have had some influence on the ERG components. Miyake et al reported a prolongation of the implicit time and a reduction in the amplitude on the intraoperative 30 Hz flicker ERGs during vitreous surgery [30,31]. Yagura et al reported a significant reduction in the amplitude and a prolongation of the implicit times of several components of the photopic ERGs after an intravitreal injection when a paracentesis was not performed [32]. They also reported that no significant differences were observed in the amplitudes and implicit times of almost all components of the photopic ERGs after an intravitreal

injection followed by the aspiration of the aqueous humor by paracentesis. Although we did not measure the IOP, we believe that the influence of the IOP was minimal because the method of injecting the agents and IOP control were performed in the same way as Yagura et al. We measured the influence of the intravitreal injection of anti-VEGF agents on the fellow eyes. Although it is possible to investigate the agent concentration and VEGF activity in the injected eye, it is not ethically possible to collect specimens from the fellow eyes. Therefore, the concentration and VEGF activity in the fellow eye were not available. In contrast, our method has an advantage of being able to evaluate the effects of the agents non-invasively. We found that there was a significant delay or a trend in the delay of the implicit times in the fellow eyes just as in the injected eye. These results suggest that anti-VEGF agents enter the systemic circulation, reach and affect the fellow eyes. Avery et al reported that the serum concentration of anti-VEGF agents increased and the plasma concentration of free VEGF decreased [28,29]. These findings are consistent with the results of our study in term of the transfer to the systemic circulation.

Although anti-VEGF agents have become a standard treatment for AMD, DME, RVO with ME, and other retinal diseases, only limited information is available concerning the influence of the anti-VEGF agents on the fellow eye especially during the early periods. Further investigations on the long-term influence on the non-injected fellow eye is needed.

Our study has several limitations. One is that some of the patients had the disease bilaterally, and the non-injected fellow eye served as a control. We compared the changes relative to the baseline in the fellow eye as well to alter the influence of the disease of the non-injected eye. However, the changes in retinal function on the non-injected fellow eye should be carefully interpreted. Further investigations on eyes with unilateral disease is necessary to strictly clarify the transfer effect of the intravitreally injected agents on the healthy fellow eye.

Second, there may be other factors that might have affected the ERGs. For example, Horiguchi et al reported on the influence of the vitreous temperature on the ERGs during vitrectomy [33]. However, we believe that the change in the vitreous temperature was probably minimal. Third, the sample size was relative small. When the eyes were classified into the different groups by agents or by diseases, the number decreased to less than 10 cases in some groups. It is necessary to collect more cases to assess the influence of each agent on the same disease or the influence on each disease with the same agent. Taking these limitations into consideration, we still believe that this study is clinically important in that we could show the influence of the agent on the injected eye as well as non-injected fellow eye in the very early postoperative period.

Conclusions

The results show that the implicit times of the flicker ERGs recorded with the RETeval system is prolonged not only in the injected eye but also in the non-injected fellow eye shortly just after an intravitreal anti-VEGF agent injection. It is necessary to evaluate the long-term influence of anti-VEGF agents of the fellow eye.

Abbreviations

anti-VEGF: anti-vascular endothelial growth factor

U.S. FDA: the United States Food and Drug Administration

AMD: age-related macular degeneration

DME: diabetic macular edema

RVO: retinal vein occlusion

ME: macula edema

ERG: electroretinography

IOP: intraocular pressure

Declarations

Ethics approval and consent to participate

All of the patients gave a written informed consent and the study was conducted in accordance with the tenets of Declaration of Helsinki and approved by the Ethics Committee of the Teikyo University School of Medicine (study ID number: 14-122).

Consent for publication

Consent for publication was obtained from the patient of Figure.1.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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was conducted at Teikyo University Hospital, and all authors have no proprietary interest.

Authors' contributions

GT and KS made the conception and design of the study and analyzed the ERG parameters. GT, KM, and HS collected and arranged the data (ERG recordings demographics, visual acuity, and date). GT made the statistical analyzes. GT, KS, SM, AM, and YM made the interpretation of data. YM gave critical comment. GT drafted the manuscript. KS was a major contributor editing it. All authors read and approved the final manuscript.

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Tables

Table 1. Number of eyes injected by disease and by injected agent.

	AMD	DME	RVO with ME	total
ranibizumab	18	18	14	50
aflibercept	19	6	3	28
total	37	24	17	78

Patient breakdown by disease and by injected agent.

AMD; age-related macular degeneration

DME; diabetic macular edema

RVO with ME; retinal vein occlusion with macular edema

Table 2. The results including all cases.

n=79 (male: 44, female: 35)			
mean age		68.9±12.6 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	31.2±3.18	31.7±3.06* p=0.0001	32.2±3.31* p=0.00000
amplitude (uV)	8.66±5.72	7.88±6.07 p=0.168	9.46±8.93 p=0.308
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	30.5±3.30	31.1±3.18* p=0.0028	31.3±3.39* p=0.00000
amplitude (uV)	9.41±6.48	9.15±6.66 p=0.618	9.51±6.19 p=0.832

The results of 28 Hz flicker electroretinogram components including all patients before classification by disease of by injected agent. The ERGs were recorded before the injection (phase 1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3).

mean ± standard deviation

*; significant difference compared with phase 1 as baseline

Table 3. The results of analyzing by disease.

Table 3-1. The ERG responses before and after injection in eyes with AMD

AMD n=37 (male: 24 female: 13)			
mean age		74.1±8.58 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	29.9±1.75	30.4±1.64* p=0.0084	30.8±2.14* p=0.00000
amplitude (uV)	8.99±5.74	8.12±6.43 p=0.402	9.04±6.34 p=0.934
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	29.5±2.46	30.4±2.11* p=0.023	30.6±2.35* p=0.00058
amplitude (uV)	10.1±7.16	9.63±7.27 p=0.635	9.81±6.18 p=0.735

Table 3-2. The ERG responses before and after injection in eyes with DME

DME n=24 (male: 14 female: 10)			
mean age		59.9±11.3 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	33.6±3.22	34.2±3.15 p=0.06	34.7±3.09* p=0.00011
Amplitude (uV)	7.95±5.88	7.05±5.83 p=0.312	7.56±5.88 p=0.319
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	33.6±3.10	34.1±3.10 p=0.109	34.3±3.40* p=0.0046
Amplitude (uV)	7.53±5.13	7.15±5.47 p=0.579	7.81±5.59 p=0.555

Table 3-3. The ERG responses before and after injection in eyes with ME associated with RVO

RVO with ME n=18 (male: 6 female: 12)			
mean age		70.1±14.9 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	30.7±3.68	31.3±3.37* p=0.038	31.6±3.79* p=0.00091
Amplitude (uV)	8.94±5.72	8.50±5.82 p=0.499	12.9±14.7 p=0.228
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	28.4±1.93	28.6±2.00 p=0.281	28.9±2.30 p=0.177
amplitude (uV)	10.5±6.43	10.8±6.47 p=0.549	11.2±6.74 p=0.320

The results of 28 Hz flicker electroretinogram components classified by disease. The ERGs were recorded before the injection (phase 1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3).

mean ± standard deviation

*; significant difference compared with phase 1 as baseline

AMD; age-related macular degeneration

DME; diabetic macular edema

RVO with ME; retinal vein occlusion with macular edema

Table 4. The results of analyzing by injected agent.

Table 4-1. The ERG responses before and after injection in eyes treated by ranibizumab

ranibizumab n=50 (male: 22, female: 28)			
mean age		68.1±13.5 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	31.6±3.45	32.0±3.45* p=0.0039	32.5±3.57* p=0.00000
amplitude (uV)	7.18±5.34	6.68±5.60 p=0.484	8.21±9.97 p=0.376
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	30.8±3.24	31.3±3.51* p=0.021	31.5±3.62* p=0.0017
amplitude (uV)	8.21±6.00	7.32±4.79 p=0.150	8.31±5.54 p=0.867

Table 4-2. The ERG responses before and after injection in eyes treated by aflibercept

aflibercept n=28 (male: 21, female: 7)			
mean age		70.1±11.0 y.o.	
injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	30.9±2.43	31.4±2.09* p=0.020	31.8±2.55* p=0.00000
amplitude (uV)	11.5±5.41	10.0±6.49 p=0.132	11.8±6.45 p=0.732
non-injected eye	Phase 1	Phase 2	Phase 3
implicit time (msec.)	30.2±3.33	31.0±2.36 p=0.058	31.3±2.85* p=0.0013
amplitude (uV)	11.7±6.86	12.5±8.23 p=0.399	11.8±6.80 p=0.923

The results of 28 Hz flicker electroretinogram components classified by injected agent. The ERGs were recorded before the injection (phase 1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3).

mean ± standard deviation

*; significant difference compared with phase 1 as baseline

Figures

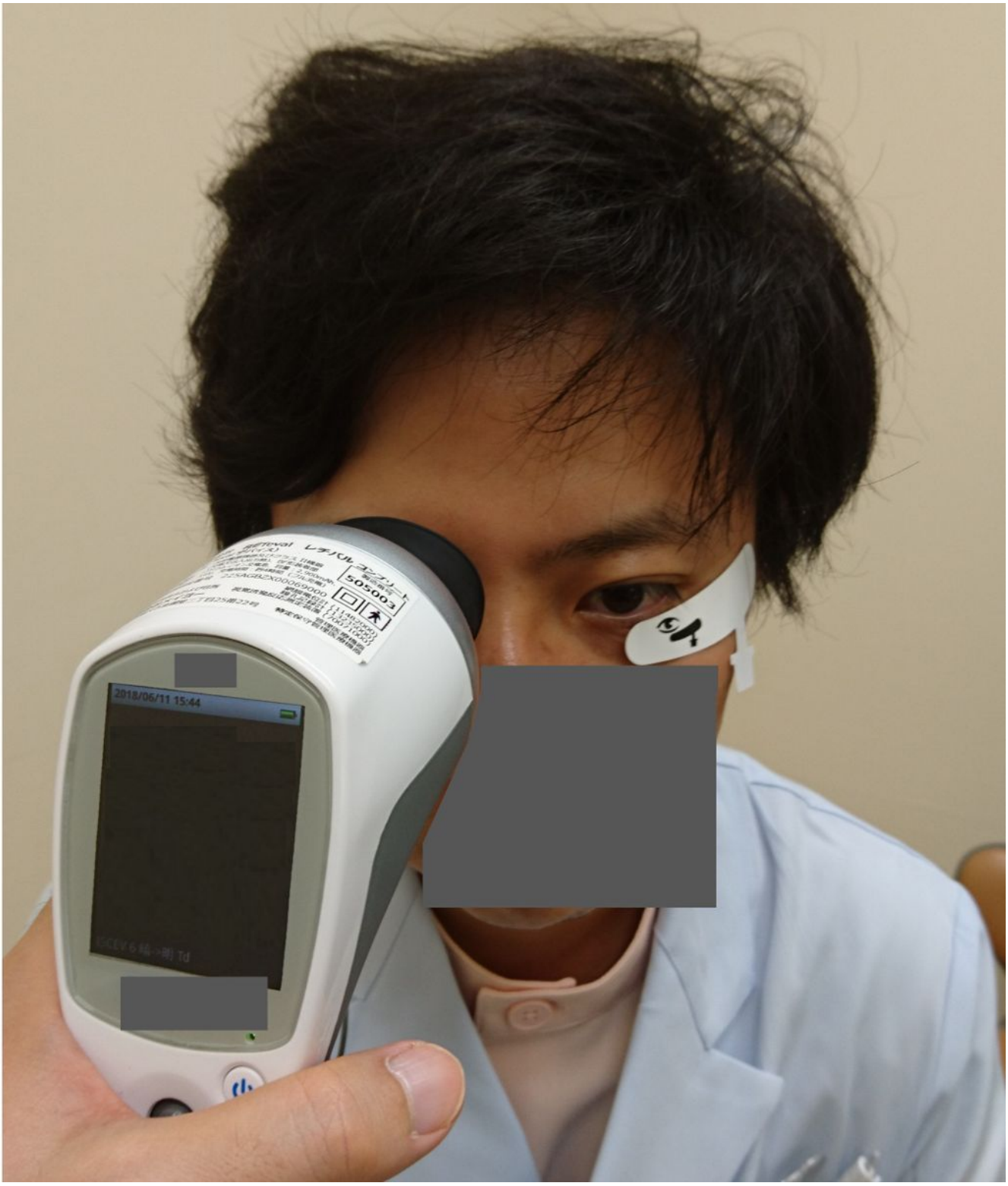

Figure 1

The image of measuring 28 Hz flicker ERG using RETeval® - The image showed that demonstration of the measuring 28 Hz flicker electroretinogram used by RETeval® under the room lighting.

(Figure 2.) The implicit time of each eye by disease.

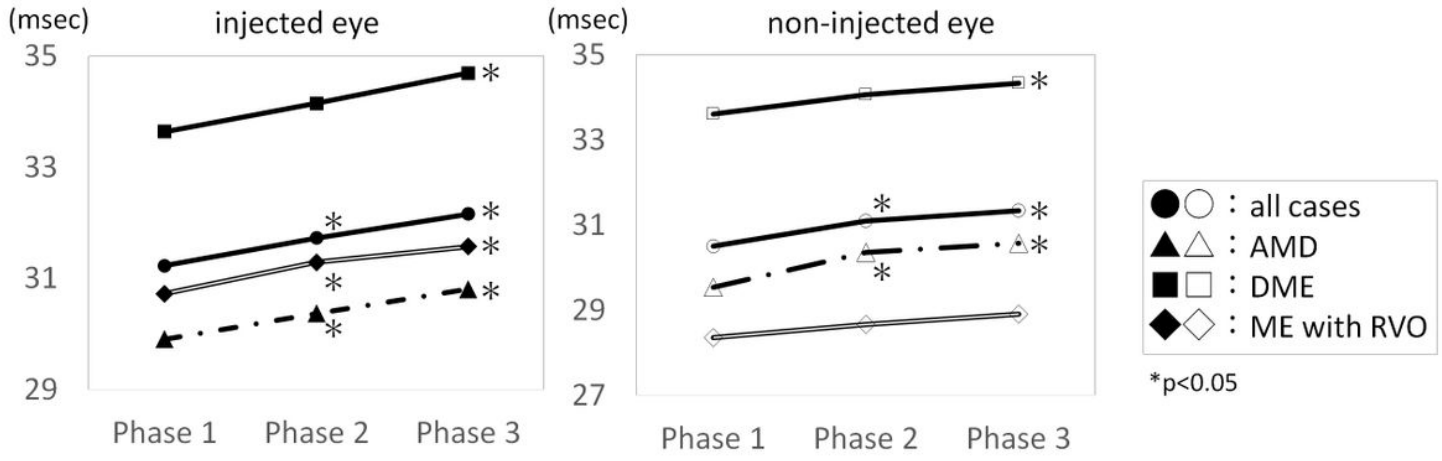

Figure 2

Implicit times of each eye segregated by disease - The graph of the implicit time of each eye segregated by disease before (phase1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3). The implicit times were significantly longer at phase 2 and 3 than at phase 1.

(Figure 3.) The implicit time of each eye by injected agent.

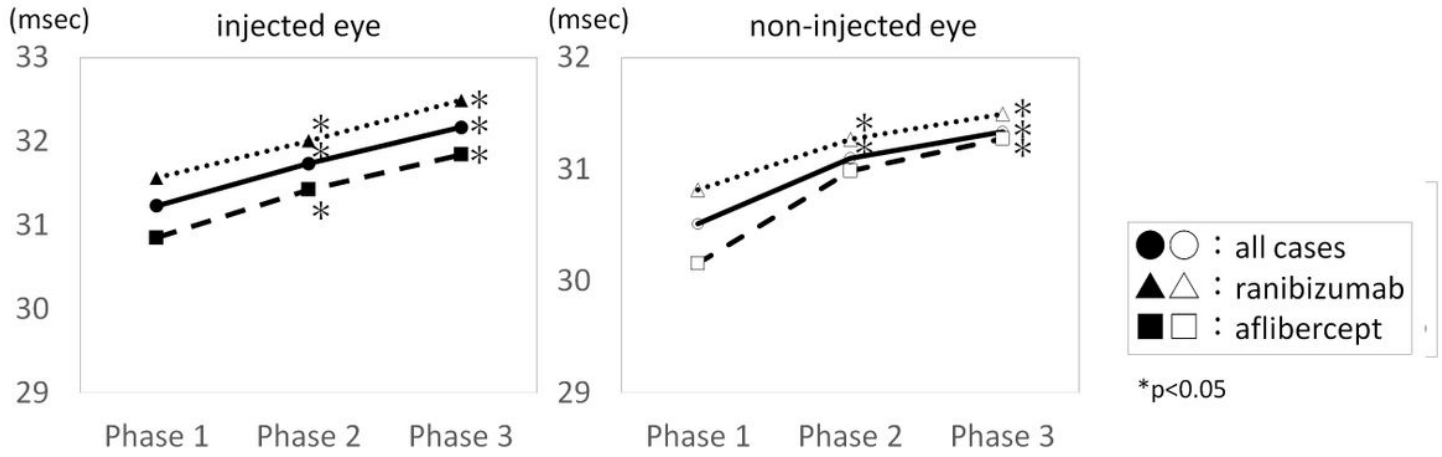

Figure 3

Implicit time of each eye segregated by the injected agent - The implicit time of each eye segregated by injected agent before (phase 1), within 2 hours after the injection (phase 2), and 2 to 24 hours after the injection (phase 3). The implicit times were longer at phase 2 and 3 than at phase 1 as the baseline. *; P <0.05