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CLINICAL INVESTIGATION

Usefulness of Anterior Chamber Depth Measurement for Efficacy Assessment of Steroid Pulse Therapy in Patients with Vogt-Koyanagi-Harada Disease

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Abstract

Purpose: To clarify the usefulness of measuring anterior chamber depth by the IOLMaster for early-stage assessment of the therapeutic effect of steroid pulse therapy in patients with Vogt-Koyanagi-Harada (VKH) syndrome with active uveitis.

Methods: Seven patients with VKH syndrome (three men and four women) participated in the study (14 eyes). All patients had exudative retinal detachment in addition to iritis, and received steroid pulse therapy: infusion of methylprednisolone (1000 mg × 3 days) followed by tapering oral administration of prednisolone (40, 30, 20, 15, 10, and 5 mg/day) over a week. Corrected visual acuity, manifest spherical equivalent, anterior chamber flare, axial length, and anterior chamber depth were measured before and after the pulse therapy. Anterior chamber flare was measured using a laser flare-cell meter, and axial length and anterior chamber depth were measured using the IOLMaster.

Results: After 1 week of steroid pulse therapy, anterior chamber depth significantly increased from the initial value of 2.94 ± 0.34 mm to 3.12 ± 0.38 mm (Wilcoxon signed-rank test, $P = 0.002$). After 1 month of steroid pulse therapy, significant changes were observed in corrected visual acuity ($P = 0.01$), manifest spherical equivalent ($P = 0.002$), anterior chamber flare ($P = 0.03$), axial length ($P = 0.02$), and anterior chamber depth ($P = 0.002$).

Conclusion: Measurement of anterior chamber depth using the IOLMaster is useful for early-stage assessment of the effect of steroid pulse therapy in patients with VKH syndrome who develop active uveitis. Change in anterior chamber depth is the most sensitive indicator of inflammatory activity in patients with this syndrome. **Jpn J Ophthalmol** 2010;54:396–400 © Japanese Ophthalmological Society 2010

Keywords: anterior chamber depth, IOLMaster, laser flare-cell meter, uveitis, Vogt-Koyanagi-Harada syndrome

Introduction

Vogt-Koyanagi-Harada (VKH) syndrome is an acute systemic syndrome first reported by Vogt, Koyanagi, and Harada.[1,2] The present opinion is that the condition is an autoimmune syndrome against melanocytes: the lesions appear in various regions where melanocytes are distributed such as the ear, inner ear, hair, and skin. Eye involvement is characterized by binocular diffuse uveitis associated with exudative retinal detachment. When iritis develops, the syndrome brings about a transient shallow anterior chamber and ocular hypertension[3] thought to be caused by ciliary edema due to inflammation. Ciliary edema in this syndrome has been detected by gonioscopy[3] and ultrasound biomicroscopy (UBM).[4–7] However, these examinations require contact between a lens and the corneal surface and hence are considered invasive to patients. A device to measure axial length by optical interferometry (IOLMaster;

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Carl Zeiss Meditec, Dublin, CA, USA) is a convenient and less invasive apparatus that can measure axial length, corneal refractive power, and anterior chamber depth without contact with the corneal surface. Although this device is widely used in clinical practice, there have been no reports so far regarding the efficacy assessment of steroid pulse therapy on VKH syndrome using this instrument. In the present study, we assessed the efficacy of steroid pulse therapy to treat VKH syndrome by time-sequential noninvasive measurement of anterior chamber depth using the IOLMaster.

Participants and Methods

The study participants were seven patients (14 eyes) who visited Kitasato University Hospital between June 2004 and October 2008 and were diagnosed (by blood tests, cerebrospinal fluid examination, and fluorescent fundus angiography) as having VKH syndrome, and who required steroid pulse therapy for the treatment of active uveitis associated with exudative retinal detachment. The patients' backgrounds, based on the guidelines announced in 2001,[8] are shown in Table 1. Steroid therapy was carried out by infusion of methylprednisolone (Solu-Medrol; Pfizer, New York, NY, USA) at a dose of 1000 mg/day for 3 days followed by oral administration of prednisolone (Predonine; Shionogi, Osaka, Japan). Oral administration of prednisolone was started at 40 mg/day, and the dose was tapered over a week (30, 20, 10, and 5 mg/day). All patients had diffuse choroiditis, and, dependent on the condition of the choroiditis, received betamethasone (Rinderon; Santen Pharmaceutical, Osaka, Japan) or fluorometholone (Flumetholon 0.1%; Santen Pharmaceutical). To prevent inflammation or posterior synechia, atropine (Nitten atropine ophthalmic solution 1%; Nitten Pharmaceutical, Nagoya, Japan) with tropicamide and phenylephrine (Mydrin-P; Santen Pharmaceutical) was used. Corrected visual acuity as logarithm of the minimal angle of resolution (logMAR), manifest spherical equivalent (D), anterior chamber flare (pc/ms), axial length (mm), and anterior chamber depth (mm) were measured before steroid pulse therapy and at 1 week and 1 month after the start of pulse therapy. Anterior chamber flare was measured with a laser flare-cell meter (FC 1000; Kowa Pharmaceutical, Tokyo, Japan), and axial length and anterior chamber depth were measured by the IOLMaster. These measurements were made during mydriasis. We conducted these measurements at least five times, and the average value was used for the statistical analysis. The Wilcoxon signed-rank test was used to compare the pretreatment and posttreatment data. A P value less than 0.05 was considered statistically significant.

Informed consent was obtained from all patients. The study adhered to the tenets of the Declaration of Helsinki.

Results

One week after the start of steroid pulse therapy, anterior chamber depth was significantly increased ($P = 0.002$), but significant changes were not found in corrected visual acuity ($P = 0.28$), manifest spherical equivalent ($P = 0.27$), flare value ($P = 0.70$), or axial length ($P = 0.18$) (Table 2).

At 1 month after the start of pulse therapy, statistically significant changes from pretreatment values were found in corrected visual acuity ($P = 0.01$), manifest spherical equivalent ($P = 0.002$), flare value ($P = 0.03$), axial length ($P = 0.02$), and anterior chamber depth ($P = 0.002$). Corrected visual acuity improved to myopia, anterior chamber flare decreased, and axial length and anterior chamber depth significantly increased (Table 2).

Table 1. Demographics of the study population

Patient	Age (years)	Sex	VKH type	Bilateral ocular involvement	Neurological / auditory findings	Integumentary finding	HLA DR4
A	53	Male	Complete	Anterior uveitis, serous retinal detachments	Headache, cerebrospinal fluid pleocytosis	Vitiligo	+
B	21	Female	Incomplete	Anterior uveitis, serous retinal detachments	Headache, malaise	−	−
C	57	Female	Incomplete	Anterior uveitis, serous retinal detachments	Headache, malaise, tinnitus, cerebrospinal fluid pleocytosis	−	+
D	43	Female	Incomplete	Anterior uveitis, serous retinal detachments	Headache, cerebrospinal fluid pleocytosis	−	+
E	65	Male	Incomplete	Anterior uveitis, serous retinal detachments	Headache, nausea, tinnitus, cerebrospinal fluid pleocytosis	−	−
F	48	Female	Incomplete	Anterior uveitis, serous retinal detachments	Headache, tinnitus	−	+
G	30	Male	Incomplete	Anterior uveitis, serous retinal detachments	Headache, malaise	−	+

VKH, Vogt-Koyanagi-Harada syndrome.

Table 2. Parameter values before and after steroid pulse therapy

Patient	Eye	Pretherapy					After 1 week					After 1 month				
		BCVA (logMAR)	SE (D)	Flare (pc/ms)	AL (mm)	ACD (mm)	BCVA (logMAR)	SE (D)	Flare (pc/ms)	AL (mm)	ACD (mm)	BCVA (logMAR)	SE (D)	Flare (pc/ms)	AL (mm)	ACD (mm)
Case 1	Right	0.22	3.75	6.9	23.44	2.76	0.15	1.50	9.1	23.65	2.92	–0.08	0.50	16.2	23.65	2.97
	Left	0.15	2.50	9.6	23.35	2.54	0.10	0.75	11.8	23.89	2.98	0.00	0.25	8.0	23.89	3.00
Case 2	Right	0.40	1.00	6.3	22.24	3.15	0.22	2.50	24.4	21.92	3.44	0.00	–1.00	12.6	22.56	3.41
	Left	0.52	1.00	9.5	21.46	3.04	0.40	2.00	20.9	22.36	3.47	0.15	–1.00	8.0	22.47	3.42
Case 3	Right	1.52	–4.58	51.7	23.32	3.15	1.52	–4.58	59.2	23.36	3.41	0.15	–6.75	10.7	24.50	3.31
	Left	0.52	–4.50	51.5	23.49	3.11	0.52	–4.50	65.4	23.66	3.17	0.15	–6.75	12.0	24.42	3.42
Case 4	Right	0.05	2.75	35.3	23.22	3.22	0.15	2.50	7.6	24.15	3.38	0.05	0.00	8.7	24.15	3.35
	Left	0.15	3.00	21.0	23.41	3.30	0.22	1.00	7.0	24.55	3.43	0.05	–0.25	5.9	24.55	3.38
Case 5	Right	0.30	3.00	62.6	22.65	2.55	0.22	4.00	26.8	23.62	2.59	0.30	0.75	9.2	24.08	3.17
	Left	–0.08	0.75	30.9	23.66	2.36	–0.08	0.00	16.1	23.54	2.43	0.05	0.50	12.0	24.11	3.18
Case 6	Right	0.00	0.25	14.2	22.25	2.40	0.22	0.75	7.3	22.01	2.54	0.00	0.25	6.4	22.80	2.70
	Left	0.40	1.50	3.4	22.12	3.40	0.15	–0.38	7.4	21.95	3.50	0.00	0.13	6.2	23.00	3.50
Case 7	Right	0.22	–2.13	5.0	22.34	2.96	0.10	–2.75	3.6	22.01	3.37	0.10	–2.25	3.4	23.70	3.55
	Left	0.15	–2.00	2.0	22.23	3.00	0.10	–3.50	3.3	22.43	3.10	0.10	–3.25	3.7	23.80	3.30
Average		0.32	0.45	22.14	22.80	2.92	0.29	–0.05	19.28	23.08	3.12	0.07	–1.35	8.79	23.69	3.26
SD		0.39	2.74	20.64	0.69	0.34	0.38	2.75	19.71	0.92	0.38	0.10	2.55	3.63	0.71	0.24
P value*		—	—	—	—	—	0.28	0.27	0.7	0.18	0.002	0.01	0.002	0.03	0.02	0.002

BCVA, best spectacle-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution; SE, spherical equivalent; AL, axial length; ACD, anterior chamber depth; SD, standard deviation.

*Compared with pretherapy values, Wilcoxon signed-rank test.

Discussion

Fluorescein angiography and indocyanine green angiography (IA) are useful for assessing the efficacy of steroid therapy in patients with VKH syndrome. In clinical practice, however, we sometimes hesitate to perform these angiographic examinations in patients who are challenged by angiography (such as pregnant women and those with poor general health status or allergy to contrast medium). Therefore, we studied the possibility of assessing the efficacy of steroid pulse therapy by measuring change in anterior chamber depth.

In the present study, 1 month after the start of steroid pulse therapy, statistically significant changes were observed in corrected visual acuity, manifest spherical equivalent, flare value, axial length, and anterior chamber depth. Of interest is that parameters showing significant changes from pretherapy levels were different between 1 week and 1 month after the start of therapy: a significant change was found only in anterior chamber depth at 1 week after the start of pulse therapy, whereas significant changes were found in all parameters examined at 1 month after the start of therapy. These results suggest that anterior chamber depth is the parameter that improves most rapidly.

Generally, in the active phase of panuveitis in patients with VKH syndrome, the anterior chamber becomes shallow owing to ciliary edema, while visual acuity decreases owing to exudative retinal detachment in the fundus (in addition to the increase in anterior chamber inflammatory cells). In 1981, Kimura et al.[3] used gonioscopy to demonstrate that patients with VKH syndrome experienced chamber angle narrowing and identified ciliary edema as its cause. Since development of ultrasound biomicroscopy (UBM), which enables observation of the anterior ocular segment in detail under physiological conditions,[9] it has been reported that ciliochoroidal detachment occurs because of accumulation of exudates in the suprachoroidal space.[4–6] Wada et al.[7] observed 14 eyes of seven patients with VKH syndrome by UBM and found chamber angle narrowing in eight eyes, ciliochoroidal detachment in five eyes, and ciliary edema in all 14 eyes. They also reported that ciliary edema was improved in all cases after 1 month of steroid therapy. In our study, an increase in anterior chamber depth in all the patients was observed after 1 week of steroid pulse therapy. Regrettably, however, UBM was not used, so whether the increase was due to improvement in ciliary body edema is not completely clear. Still, all patients in this study had diffuse choroiditis accompanied by acute iritis and serous detachment (Table 1). In addition, the above-mentioned reports[4–7] suggest that ciliary body edema and its improvement may be associated with an increase in anterior chamber depth. Thus, it is known that chamber angle narrowing due to ciliary edema takes place in the active phase of VKH syndrome, and the morphology of the lesions can be observed in detail. However, because goniotomy and UBM require use of a cornea-contacting lens and the examination takes a rather long time, these tests are problematic for patients and observers.

The IOLMaster is an instrument capable of measuring axial length, corneal refractive power, and anterior chamber depth without physical contact with the cornea. The device measures the distance between the corneal surface and retinal pigment epithelium by applying the principle of optical interference using a feeble diode-laser light source (780 nm). Since measurement can be done without corneal contact, there is no need for topical anesthesia or preventive measures against infection, and there is no corneal stress. Another advantage to this method is that the measurement can be done quickly (time for laser irradiation, 0.5 s; measurement time, 1 min). The reproducibility of the measurement is good: Verhulst and Vrijghem[10] reported that the instrument gave good results with little refractive error in patients undergoing cataract surgery. The one shortcoming of the instrument is that measurement is difficult if a patient has severe opacity in the anterior ocular segment or of the transparent ocular media because it uses a fine laser beam. Although all of the patients in the present study had exudative retinal detachment as well as iritis, their visible patterns were good and there were no problems in measurement.

The IOLMaster could detect an increase in anterior chamber depth as a significant change even 1 week after the start of steroid pulse therapy. This improvement may indicate that a shallow anterior chamber due to ciliary edema or ciliochoroidal detachment was improved by the anti-inflammatory action of the steroids. Traditionally, anterior chamber inflammation is evaluated in terms of the grading of flare and cells by using slit-lamp microscopy[11] or a laser flare-cell meter. However, the former is considered to be a semiquantitative method because it is less sensitive and it is difficult to standardize intraobserver and intrainstrumental variations. The latter is a method that measures the severity of anterior chamber inflammation as a continuous variable, and reproducibility was shown to be high in an in vivo experiment[12] and an in vitro measurement.[13] However, it is difficult to monitor the time-course change of chronic inflammation by this method. The laser flare-cell meter is said to be good at measuring anterior chamber flare intensity. In the active phase of uveitis, the blood–aqueous barrier is disrupted and the protein concentration in the aqueous humor rises, and this rise is associated with anterior chamber flare. However, it has been reported that improvement of anterior chamber inflammation by anti-inflammatory treatment does not result in immediate correction of the flare value, as the disrupted blood–aqueous barrier is not quickly restored.[14] We also could not find a decrease in the flare value after 1 week of steroid pulse therapy in the present study. The flare value significantly decreased after 1 month of therapy, although the anterior chamber depth changed as early as 1 week after therapy. Therefore, anterior chamber depth may be a more sensitive indicator of anterior chamber inflammation in patients with VKH syndrome.

Subjects in this field needing future study include exact measurement of anterior chamber depth and cross-evaluation of data obtained by measurement of anterior chamber depth and angiography (e.g., IA) and UBM for evaluation of choroidal circulation. Recently, a novel instrument for measuring anterior chamber depth, the AC Master (Carl Zeiss Meditec) has been introduced. Meinhardt et al.[15] comparatively measured anterior chamber depth by the AC Master, IOLMaster, Pentacam (Oculus, Lynnewood, WA, USA), and Jaeger (Haag-Streit International, Koeniz, Switzerland) and reported that the AC Master showed the highest reproducibility. Evaluation of the reliability of the AC Master is needed and it may be a candidate for further study. It has also been reported that fundus angiography is useful for efficacy assessment of steroid therapy.[16,17] However, IA and UBM were not regularly performed in the participants in the present study. It will be necessary to assess the choroidal circulation by IA and the morphology of the ciliary body by IA and UBM and to clarify the relationship between these findings and anterior chamber depth. Furthermore, with the advent of anterior segment optical coherence tomography (OCT), it has now become possible to obtain a clear image of the anterior segment in a noncontact way within a short time. Zhang et al.[18] have reported in detail on corner shapes in patients with acute primary angle closure, and Aptel and Denis[19] have reported on changes in iris shape accompanied by mydriasis. In both studies, the procedures were less invasive for patients, with more detailed information than previously on the shapes of the anterior segment. In the future, we think it will be possible to capture in more detail the changes in the iris shape of patients with VKH disease by using anterior segment OCT. In addition, further study with a larger subject population is necessary, as the sample size of the present study was small.

The present study results suggest that change in anterior chamber depth is the most sensitive indicator of inflammatory activity in patients with VKH syndrome. It also suggests that the IOLMaster, which is convenient for measurement and less invasive, is useful for efficacy evaluation of steroid therapy in patients who have difficulty undergoing angiography, such as patients with poor general health status, those allergic to contrast media, and pregnant women.

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