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ORIGINAL PAPER

Assessment of Schlemm's canal in acute primary angle closure: an anterior segment optical coherence tomography study

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Abstract

Purpose To image and quantitatively evaluate the Schlemm's canal (SC) dimensions in the eyes with acute primary angle closure (APAC) with anterior segment optical coherence tomography (AS-OCT), and compare it with the SC measurements taken after the control of intraocular pressure (IOP) and in the normal age-matched controls.

Materials and methods Seventeen eyes of 14 patients with the newly diagnosed APAC and 59 age-matched normal subjects underwent AS-OCT to image SC. SC cross-sectional area, SC meridional and coronal diameters were measured in the temporal and nasal regions at 3 and 9 o'clock position. After laser iridotomy and control of the IOP, all SC parameters were measured again at a week later, in APAC eyes. Intrasession intraobserver reliability of the SC measurements was assessed with intraclass correlation coefficient.

Results Mean SC-SCA (10,600 ± 2691 μm^2), SC meridional (682 ± 125 μm) and coronal diameters (21.2 ± 8.2 μm) showed a significant increase in the APAC eyes at presentation, when compared to the SC parameters measured at a week later (6499 ± 1754 μm^2, 450 ± 169 μm and 15.75 ± 8.6 μm, $p = < 0.0001$, < 0.0001 and 0.01, respectively) and in the normal controls (7192 ± 1022 μm^2, 499.2 ± 179.8 μm, 15.43 ± 4.35 μm, $p = 0.02$, < 0.0001, 0.01, respectively). There was no difference in the measured SC parameters between the normal controls and APAC eyes, when the parameters were measured at a week, after resolution of the acute attack (all $p > 0.05$).

Conclusion A significant expansion of SC was observed in the APAC eyes at presentation, when compared to the normal controls and after the acute attack resolved. SC parameters may provide a useful research tool for evaluating morphological changes in the SC in APAC eyes, during an acute attack.

Keywords Acute primary angle closure · Anterior segment optical coherence tomography · Schlemm's canal

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Introduction

Schlemm's canal (SC) is an unique, endothelial-lined, circular vessel, located at the inner aspect of the corneo-scleral junction and plays an important role in the aqueous humour outflow through the conventional trabeculo-canalicular pathway and in the maintenance of normal intraocular pressure (IOP) [1].

Anterior segment optical coherence tomography (AS-OCT) is a non-invasive, high-resolution device, which allows in vivo imaging of the SC [2–5]. Previous studies using AS-OCT have demonstrated that an acute elevation of IOP causes a reduction in the SC size due to collapse of SC, resulting in an increased aqueous outflow resistance [6, 7].

We measured the SC dimensions with RTVue AS-OCT (Optovue, Inc, Fremont, CA, USA) in the acute primary angle closure (APAC) eyes at presentation and compared it with the SC measurements taken at a week later, after the laser peripheral iridotomy (LPI) and control of IOP and also with the age-matched normal controls.

Materials and methods

This prospective comparative study included 14 newly diagnosed eyes of APAC (3 patients had bilateral acute attack) and 59 age-matched normal participants, who had come to the institute between August 2017 to February 2018. The study followed the tenets of the Declaration of Helsinki, and all the participants gave informed consent for the study.

All subjects underwent comprehensive ophthalmic examination, including medical and ocular history, best-corrected visual acuity, refraction, slit lamp biomicroscopy, IOP measurement with Goldmann applanation tonometry, gonioscopy with Sussman goniolens, undilated fundus evaluation in patients with APAC and later post-dilated fundus examination after LPI. Central corneal thickness (CCT), central anterior chamber depth (ACD) and axial length (AL) were measured with AL-scan (Nidek, Gamagori, Japan). AS-OCT was performed with RTVue AS-OCT, at the time of initial presentation, and was repeated at a week later, after the acute attack had resolved and IOP was controlled with the anti-glaucoma medications (AGM) and LPI. In the normal subjects, one eye was randomly selected for the data analysis.

APAC was defined as a sudden onset of ocular pain, associated with at least 2 symptoms: headache, sudden decrease in vision, nausea and/or vomiting and at least 3 of the following signs: circumcorneal ciliary congestion, corneal oedema, shallow AC, mid-dilated pupil, IOP > 25 mmHg and glaukomflecken. Normal participants were of age > 40 years, spherical equivalent of $\pm$ 2 diopters, IOP < 20 mmHg, open angles on gonioscopy, unremarkable anterior and posterior segment examination and no history of ocular trauma, ocular pathology or surgery.

Data acquisition and processing

All the eyes underwent scanning with RTVue AS-OCT, by an experienced operator using corneal line scan (8 mm scan length), placed on the limbus, in the nasal and temporal horizontal meridian (3 and 9 o'clock position). Patients were asked to look at an external fixation target with the fellow eye. All the scans were repeated thrice, and the images with poor resolution, motion artefacts, excessive noise or shadowing were discarded. Based on the image quality, only one image was chosen for the final analysis. During the follow-up examination, efforts were made to obtain scans in the same region of limbus using conjunctival vessels as a landmark.

In the cross-sectional image, SC was identified as a horizontally oval- or elliptic-shaped black translucent space, close to the trabecular meshwork (TM) (Fig. 1a). The AS-OCT images of the SC were exported using OCT files and were opened using image J 2 tool (https://imagej.nih.gov/ij/plugins/raw-file-opener.html). To improve visualization of the SC, file rotation, and de-noising was done. Using the free hand option specified in the tool, SC (yellow outline) was marked by a single experienced examiner, who was masked to the clinical diagnosis. SC cross-sectional area (SC-CSA) was measured by fitting optimal ellipse to the SC-CSA, and SC meridional diameter (diameter of SC measured from anterior to posterior end point of the SC) and coronal diameter (defined as the maximum distance between the inner and outer wall of SC-CSA) were also measured (blue lines). The tool computes the measurements based on the markings provided (Fig. 1b).

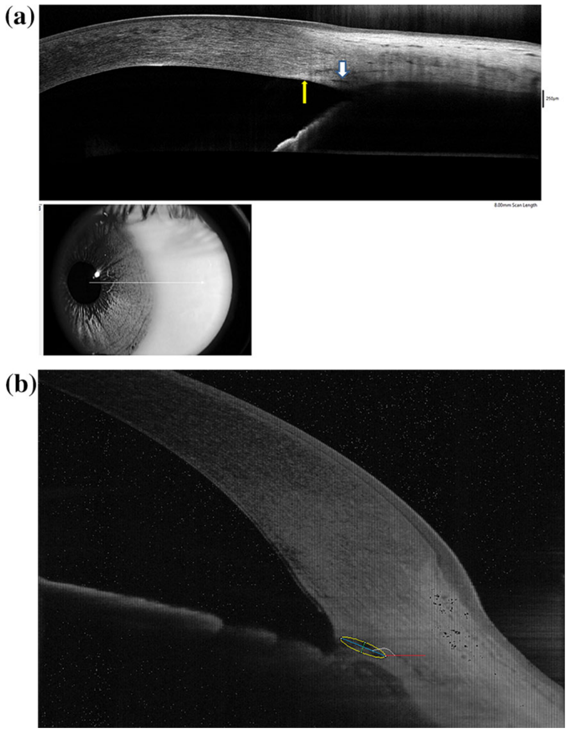

Fig. 1 **a** Anterior segment optical coherence tomography image of the Schlemm's canal (white arrow) in a normal subject in the temporal quadrant, seen as black, translucent, horizontally oval space. Yellow arrow shows termination of the Schwalbe's line. **b** Schlemm's canal (SC) measurements using image J software. SC is marked with yellow, vertical line represents coronal diameter, and horizontal line represents meridional diameter (blue colour)

Statistical analysis was performed using SPSS software version 16 (SPSS Inc., Chicago, IL, USA) Descriptive analysis is presented as mean ± standard deviation. Levene's test was used for the equality of variances, and comparison between the groups was made using independent sample student *t* test. A *p* value of < 0.05 was considered statistically significant. Intraobserver repeatability of SC measurements was tested using intraclass correlation coefficient (ICC) for the three consecutive SC scan measurements obtained in a single session in the 9 normal and 5 APAC eyes.

Results

Seventeen eyes of 14 patients with the newly diagnosed APAC underwent AS-OCT at presentation and at a week after the resolution of an acute attack. Ten were right eyes, and 7 were left eyes. Fifty-nine age-matched subjects were enrolled as normal controls. Baseline characteristics of the study participants are shown in Table 1. All the APAC patients were females, and there was no significant difference in the age ($p = 0.334$), CCT ($p = 0.86$), AL ($p = 0.09$) between the APAC patients and normal age-matched controls. The eyes with APAC had a higher IOP ($p < 0.0001$) and worse visual acuity ($p = 0.001$), compared with the normal controls. There was no significant difference in the IOP in normal group and APAC eyes (15.2 ± 4.8 mm Hg, $p = 0.09$) at a week after the control of IOP.

SC was clearly visualized in all the normal eyes and 80% of the APAC eyes, in the obtained scans sections. In 20% of the initial scans in APAC eyes, the border of SC appeared a bit fuzzy, but the SC could be identified and the scans were repeated till good quality images were obtained. It was a little difficult to obtain the scans in patients with bilateral APAC, because of the poor fixation. However, all scans could be obtained without any major discomfort to the patients.

Intrasession intraobserver ICC was 0.95 for the SC-CSA, 0.929 for the SC meridional diameter and 0.749 for the SC coronal diameter in the normal eyes. In the APAC eyes, intraobserver ICC was 0.85 for the SC-CSA, 0.82 for the SC meridional diameter and 0.76 for the SC coronal diameter. This indicates good reliability for all the SC measurements, as measured with AS-OCT.

APAC eyes had significantly increased SC-CSA (10,600 ± 2691 μm^2 vs. 7192 ± 1022 μm^2, $p = 0.02$), SC meridional diameter (682 ± 125 μm vs. 499 ± 179.8 μm, $p < 0.0001$) and coronal diameter (21.2 ± 8.2 μm vs. 15.4 ± 4.3 μm, $p = 0.01$) during the acute attack, when compared to the normal controls. (Table 2, Fig. 2a) SC-CSA (6499 ± 1754 μm^2, $p < 0.0001$), SC meridional diameter (450 ± 169 μm, $p < 0.0001$) and coronal diameter (15.7 ± 8.6 μm, $p = 0.01$) had significantly decreased at a week later, after the LPI and control of IOP with the AGM (Fig. 2b), and all the SC parameters were comparable to normal control eye (Table 2).

There was no significant difference between the measurements of the nasal and temporal scan section SC parameters in normal as well as the APAC eyes (Table 3).

Table 1 Baseline characteristics of the study participants

Variables	Normal eyes (n = 59)	Acute angle closure glaucoma eyes (n = 17)	p values
Age (in years)	54 ± 1.55	53.35 ± 1.32	0.15
Gender (male:female)	9:50	0:14	0.19
Intraocular pressure (mmHg)	14.28 ± 5.7	36.86 ± 7.99	< 0.0001
Central corneal thickness (μm)	506.64 ± 18.54	505.71 ± 12.87	0.86
Central anterior chamber depth (mm)	2.9 ± 0.4	2.45 ± 0.39	0.0003
Axial length (mm)	22.9 ± 0.4	22.7 ± 0.39	0.09

Table 2 Comparison of anterior segment optical coherence tomography measured Schlemm's canal parameters of normal eyes, acute primary angle closure (APAC) eyes and post-treatment APAC eyes after 1 week

Parameters	Normal control eyes[a]	Acute primary angle closure (APAC) eyes[b]	APAC eyes after laser iridotomy and IOP control (after a week)[c]	p value[a,b]	p value[b,c]	p value[a,c]
Mean SC area (μm^2)	7192 ± 1022	10,600 ± 2691	6499 ± 1754	0.025	< 0.0001	0.85
Mean SC diameter horizontal (μm)	499.2 ± 179.8	681.9 ± 124.8	499.8 ± 169.3	< 0.0001	< 0.0001	0.99
Mean SC diameter vertical (μm)	15.43 ± 4.35	21.22 ± 8.19	15.75 ± 8.6	0.011	0.015	0.86

IOP Intraocular pressure

[a,b] P values between APAC and normal age-matched control

[b,c] P values between APAC eyes and after resolution of APAC attack

[a,c] P values between normal and in patients after resolution of APAC

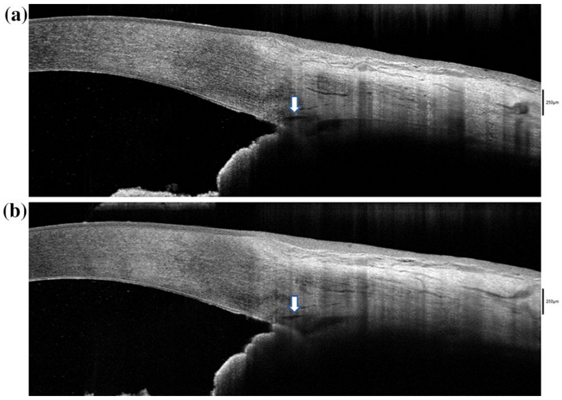

Fig. 2 Anterior segment optical coherence tomography images of the Schlemm's canal (white arrow) in an eye with acute primary angle closure, at presentation (**a**) and at a week after the resolution of acute attack (**b**)

Discussion

We quantitatively measured the SC parameters in vivo, in the eyes, after an acute attack of PAC using AS-OCT. A significant increase in the SC-CSA and SC diameter was found after the APAC, which were noted to decrease in the size and area and were comparable to the values, as seen in the normal controls and the SC parameters at a week after resolution of the acute attack.

The measured SC parameters had good intrasession intraobserver reliability of measurements in the normal eyes. Kagemann et al. [3] reported a CV of 11.4% in healthy subjects for the SC-CSA between two observers. Another study showed that the SC diameter and area measurements by RTVue AS-OCT (Optovue Inc, Toledo, OH) had good intra- and inter-observer repeatability in the primary open angle glaucoma (POAG) patients [8].

Table 3 Comparison of anterior segment optical coherence tomography measured Schlemm's canal parameters in the nasal and temporal section parameters of the normal and acute primary angle closure eyes

Parameters	Normal control eyes	Acute Primary angle closure eyes
Schlemm's canal (SC) area (μm^2)		
Temporal quadrant	6130 ± 1541	11,411 ± 2807
Nasal quadrant	5779 ± 2609	9462 ± 2215
p value	0.215	0.148
SC meridional diameter (μm)		
Temporal quadrant	507.2 ± 203.41	681.6 ± 99.72
Nasal quadrant	493.4 ± 163.14	682.3 ± 163.13
p value	0.773	0.992
SC coronal diameter (μm)		
Temporal quadrant	16.4 ± 50.1	23.03 ± 95.5
Nasal quadrant	14.71 ± 37.16	19.94 ± 49.5
p value	0.143	0.221

Using AS-OCT, Kagemann et al. [3] found that the SC area in normal subjects was significantly larger on the nasal side than on the temporal side (10, 983 μm^2 vs. 8308 μm^2). Hong et al. [8] measured the SC area and diameter using customized software of RTVue AS-OCT and found larger SC area in the temporal section than the nasal section of normal and POAG patients, but the difference was not statistically significant. Also, there was no difference in the diameter of SC in normal and POAG eyes in the nasal and temporal sections. Another AS-OCT study [4] reported that the differences in the SC parameter measurements were not statistically significant between temporal and nasal sections of the eye. In our study, we did not find any significant difference between the nasal and temporal SC measured parameters in the normal as well as in the APAC eyes.

In a histopathological study, the trabecular specimen of 16 PACG patients (6 with acute PACG and 10 chronic PACG) was examined by light and electron microscopy [9]. In acute PACG, the TM showed generalized oedema and pigments accumulation in the widened trabecular spaces and SC. In the eyes with chronic PACG, the TM revealed fewer and narrower trabecular spaces with fusion of the trabecular beams. Sihota et al. [10] studied ultrastructural changes in the TM of acute PACG eyes by scanning electron microscopy and found that the TM has grossly swollen, irregular trabecular endothelial cells, numerous activated macrophages, leucocytes and amorphous debris. It was thought that the marked oedema of the endothelium probably contributes to the acute and marked elevation in IOP.

A previous study using AS-OCT has shown that the SC- CSA is reduced by 50% after acute IOP elevation (with ophthalmodynamometer, set at a 30 g force) in the healthy eyes due to the SC compression [6]. Another study found a reduced SC-CSA, diameter and perimeter in the POAG patients [8, 11, 12]. The SC coronal diameter correlated with the IOP in POAG eyes, and the authors speculated that the SC meridional diameter was an indicator that reflects that the SC did not collapse in glaucoma [12]. Allingham et al. [7] reported a statistically significant correlation between SC area and the aqueous outflow facility. The POAG eyes had a significantly smaller SC-CSA and SC perimeter when compared with the normal eyes, which may have accounted for approximately half of the decrease in outflow facility.

Kagemann et al. [2] reported an average SC-CSA of 7614 ± 2162 μm^2 in the healthy eyes with Cirrus AS-OCT (Zeiss, Dublin, CA, USA). In another study, [3], the SC area was found to be 12,890 μm^2 in the scans near collector channel junctions, and they reported that the SC-CSA varies along its arc, within a short distance. Usui et al. [4] showed that the location of OCT scan line, its depth direction reference position and the relative position to the OCT system light can impact the SC imaging and reported the SC to be 350 μm long in its meridional axis. With the RTVue OCT device, Hong et al. [8] demonstrated the average SC area of 13,991 ± 1357 μm^2 and SC diameter of 45.2 ± 4.0 μm in normal eyes. In our study, we found the mean CS-CSA to be 7192 ± 1022 μm^2 meridional diameter to be 499.2 ± 179.8 μm and coronal diameter to be 15.43 ± 4.35 μm in the normal eyes. The difference in the dimensions measured could be because of the customized software which was used for the measurement by Hong et al. [8], the population studied and the position of the line scan at the limbus.

The histological studies [9, 10] in the PACG eyes have studied trabecular specimen from the patients who underwent trabeculectomy and were on maximal tolerated AGM before the surgery. Previous AS-OCT studies have measured SC parameters in patients with chronic PACG, in whom the IOP was controlled with AGM, which can have an affect on the morphology of SC [13, 14].

In an electron microscopy study, AC angle of 10 enucleated human eyes of secondary ACG was examined and it was found that in some of the cases with complete angle closure, extending up to the peripheral cornea, SC was widely dilated and it was assumed that the total abolition of aqueous flow resulted in the blood reflux from the collector channels which were under high pressure, due to episcleral congestion (secondary to the raised IOP) [15]. It was postulated that with the rise in the IOP, the TM tissue will be protected in the sectors with complete irido-trabecular contact, whereas in the areas with narrow synechiae the TM would be exposed to high flow of aqueous due to the high IOP.

Our study probably looks at the physiological status of SC during an acute attack of PAC, as the imaging was performed when the patients had first presented to us. We speculate that the increased SC area and diameters may be related to the swelling and expansion or distension of SC due to sudden increase in IOP in the APAC eyes. After the acute attack resolved, the SC dimensions comparatively reduced in the size, which could possibly mean that SC regains its original area and size after IOP reduction.

The pathological effect of sudden increase in the IOP has not been reported in the APAC eyes at the onset of acute attack. There is a possibility that the SC response to the acute and chronic rise in the IOP may be different. Also, there may be a difference in the SC response to the acute rise in IOP in the healthy eyes with open angles (when IOP is increased in the healthy eyes) [6] and in the APAC eyes, where the eyes are anatomically disposed for the angle closure. We speculate that in response to a sudden rise in IOP, the SC compensates by distension as compared to its response in the chronic rise in IOP, where the SC has been reported to be compressed and reduced in dimensions. Another possibility is that the collector channel (CC) junctions are also dilated in the APAC eyes and scan of SC has included the CC junction. However, this cannot explain an increase in the coronal diameter of the SC. Thus, in all the probability, we are looking at the SC dimensions in the APAC eyes, without inclusion of the CC junction.

Limitation of our study is the small number of APAC eyes. Second, we examined only 2 scans of the SC in 2 quadrants, which may not represent overall change in the SC. Whether a single-scan measurement can represent the overall SC dimensions needs further investigation. Although, we found no statistically significant difference in the nasal and temporal section parameter measurements, both in the normal and APAC eyes. Third, we did not assess the impact of AGM on SC measurements, which might have affected the SC measurements after lowering of IOP in APAC eyes. Fourth, though we made an attempt to ensure that all the scan were obtained at the same location of limbus during follow-up, using conjunctival vessels as a landmark, due to the lack of eye tracking imaging with the AS-OCT, it is not possible to obtain the consecutive scan at the exact location. Fifth, inter-operator variability of SC measurements was not measured as all the scans were measured by a single operator.

To conclude, we have demonstrated, reliable, in vivo morphological changes in the SC in APAC eyes during an acute attack and after the resolution of the attack, using AS-OCT. Non-invasive measurements of the SC parameters may provide a useful research tool for evaluating the morphological changes in SC in APAC eyes. Further studies with larger sample size are needed to validate the anatomical alteration in the SC in response to a sudden increase in the IOP.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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