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Journal of Nanjing Medical University, 2007, 21(4): 262-267
www.elsevier.com/locate/jnmu
Research Paper

The effect of lens parameters on the development of the primary angle-closure glaucoma☆

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Received 26 February 2007

Abstract

Objective: To investigate the role the lens dimensions played on the pathogenesis of primary angle-closure glaucoma. **Methods**: 38 eyes of 20 patients with primary angle-closure glaucoma (PACG) and 35 eyes of 22 normal individuals without ocular abnormalities were examined. The anatomical parameters of the lens and other structures of the anterior segment were calculated using B ultrasound, computer image processing and ultrasound biomicroscopy (UBM). The parameters were compared between the patients and normal subjects. Correlation analysis was used to determine the relationship between the radii of curvature of the anterior lens surface (RCALS) and the other parameters of the anterior segment. **Results**: Compared with the normal eyes, the eyes of PACG had thicker lens, steeper curvature of anterior lens surface, decreased depth of the anterior chamber, narrower chamber angle, and more anterior position of the ciliary bodies and lens. All these differences were significant ($P < 0.05$ or $P < 0.01$). In the PACG group, the RCALS had significantly negative correlation with the central and peripheral lens thickness ($P < 0.01$ and $P < 0.05$ respectively), and had positive correlation with relative lens position, anterior chamber depth (ACD), angle-open distance at 500 um (AOD_{500}), trabecular iris angle (TIA) and trabecular ciliary processes distance (TCPD, $P < 0.05$ or $P < 0.01$). **Conclusion**: The occurrence of PACG is relevant to the abnormal anatomical structures of the anterior segment. Among all factors, the lens parameters play an important role in the pathogenesis. Increased lens thickness, relative more anterior position of lens, especially steepened curvature of anterior lens surface are predisposing factors of the pathologic phenomenon in PACG including pupillary blockage, shallow anterior chamber, secondary closure of chamber angle and elevation of intraocular pressure.

Keywords: primary angle-closure glaucoma; lens dimensions; ultrasound biomicroscope; mechanism

INTRODUCTION

Glaucoma is the second cause of blindness after cataract and the most common irreversible blindness. Primary glaucoma is a main form of glaucoma. There is high incidence of primary angle-closure glaucoma (PACG) in Asia, especially in China. So far, the pathogenesis of PACG is not fully understood. Previous research has confirmed that many anatomical factors of anterior segment predispose individuals toward PACG, such as microcornea, shallow anterior chamber depth, increased lens thickness, shorter axial lengths *et al* [1-4]. About the effect of the lens parameters on the pathogenesis of PACG, previous articles paid more attention on the thickness and relative position of lens, lacking of systemic investigation. In order to further understand the mechanism of PACG, this study investigated the

☆This work was supported by Science and Technology Foundation of Shanxi Province [No: 2005K12-G(3)]

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role of the lens dimensions playing on the pathogenesis of PACG from the aspects such as the central and peripheral lens thickness, relative position of lens and the RCALS and so on.

MATERIALS AND METHEDS

This study included patients with PACG hospitalized in our ophthalmology department from November 2005 to November 2006 and randomly selected normal individuals. Informed consent was obtained from all participants, and the study was approved by the Institutional Review Board of the Medical College of Xi'an Jiaotong University. The research adhered to the tenets of the Declaration of Helsinki.

Patients

A total of 20 inpatients (38 eyes) diagnosed with PACG were selected. The diagnosis was based on the comprehensive ophthalmologic examination and medical records, according to the criteria described by the Chinese Medical Association for Glaucoma in 1987. Among all the cases studied; 15 (29 eyes) were acute angle-closure glaucoma, including 10 eyes of latent stage, 9 eyes of attack stage; 7 eyes of intermittent stage, 2 eyes of chronic stage and 1 eye of absolute stage; 5(9 eyes) were chronic angle-closure glaucoma, including 3 eyes for each of the early, intermediate and late stages respectively. The average age was (64.7 ± 7.83) years (range, 53 to 81 years) with 12 female (22 eyes)and 8 male (16 eyes). Based on the purpose of this investigation, patients with PACG were excluded from investigation if: ① they were incorporated with other ocular diseases or with moderate to severe refractive error or underwent any operations of anti-glaucoma before. ② miotic was used in a latest week.

Normal control group

The control group consisted of 22 volunteers (12 female:19 eyes;10 male:16 eyes) who were free from any ocular disease including moderate to severe refractive error. The average age was (65.2 ± 9.53) years(range, 53 to 85 years).

Statistical analyses showed that there was no significant difference in sex ($\chi^2 = 2.62, P > 0.05$, chi-square test) and in age ($t = 0.958, P > 0.05$, t-test) between two groups.

The parameters of lens

A B-mode color duplex diagnostic scanner (Sequoia TM 512; Acuson Corporation; Mountain View, CA) with an 8-MHz linear array scan head and a resolution of 0.5mm was used throughout this study to measure the lens parameters. During the examination, the patients were in a supine position with both eyes closed and were instructed to keep their eyes in a forward-viewing position and remain as immobile as much as possible. Ultrasound probe was put on closed eyelids with no added pressure to the eyes. Lens images with maximum horizontal length were selected to be saved(3 images per eye). In the measurements of central lens thickness(CLT), peripheral lens thickness (PLT), lens diameter(LD) and axial length of eyeball (AL), each parameter was measured 3 times and the median value taken. PLT is defined as the median thickness of two sides 3mm peripheral from the centre of lens. The RCALS, radii of curvature of posterior lens surface (RCPLS), lens volume (LV) were calculated from the saved lens image using the author self-developed software with each eye being computed three times to obtain the median value. Relative lens position (RLP) was measured as the method described by Lowe[5](i.e., ACD +1/2 lens thickness)/axial length.

Other anatomical parameters of the anterior segment

Scanning was performed using the Zeiss-Humphrey ultrasound biomicroscope (UBM, Model P40, Paradigm®, Humphrey-Zeiss, San Leandro, CA, USA). This instrument consisted of a 50 MHz transducer probe, allowing 4-5 mm tissue penetration and approximately 50 μm resolution. The examinations were performed with the patient in the supine position. After surface anesthesia, an eye cup was used to separate the eyelids, filled with 2% methylcellulose as a coupling medium. Scanning was performed to describe the anterior segment configuration and the images were saved onto hard disc, according to Pavlin's criteria [6]. Using the installed program in UBM, the anterior chamber depth (ACD) was measured 3 times as an axial distance from the internal corneal surface to the lens surface, and the median value was used; The following variables of each eye were measured at 4 positions (12:00, 3:00, 6:00 and 9:00 o'clock respectively): Angle opening distance at 500 μm from the sclera spur (AOD500), trabecular iris angle(TIA), and trabecular ciliary processes distance (TCPD). The median value was calculated from the values at all four measured positions. All UBM examinations were carried out by a single examiner with extensive UBM experience.

Statistical analysis

We used SPSS13.0 software(SPSS Inc., Chicago, Illinois, USA) to perform the statistical analyses.

T-test was performed for detecting the difference between the parameters in the groups. The correlation between the parameters was calculated with the Pearson method. A value of P <0.05 was considered to be statistically significant.

RESULTS

Comparison of the lens parameters between PACG eyes and control eyes

Comparing to the control eyes, the PACG group had increased central and peripheral lens thickness ($P < 0.01$). Relative lens positions were statistically different between the two groups($P < 0.05$) with the PACG group being apparently anterior. The PACG group had a steeper curvature of anterior lens surface than the control group ($P < 0.001$). In comparison with control group, the average lens diameter and lens volume of the PACG group were larger, while the mean RCPLS was smaller. However, the difference was not significant($P > 0.05$)(***Tab 1***, ***Fig 1,2,3 and 4***).

Tab 1 **Comparison of the lens parameters between two groups** ($\bar{x} \pm s$)

parameters	PACG group (n = 38)	Control group (n = 35)	T value	P value
CLT (mm)	4.71 ± 0.36 (4.1 – 5.8)	4.45 ± 0.32 (4.0 – 5.2)	3.023	0.004
PLT (mm)	3.44 ± 0.33 (2.9 – 4.2)	3.22 ± 0.27 (2.7 – 3.7)	2.911	0.005
lens diameter (mm)	10.74 ± 0.57 (9.6 – 12.5)	10.63 ± 0.63 (9.7 – 12.4)	0.746	0.459
RCALS (mm)	8.30 ± 1.76 (6.58 – 11.67)	10.38 ± 2.45 (7.33 – 14.66)	−4.771	0.000
RCPLS (mm)	5.88 ± 0.71 (5.08 – 6.88)	5.98 ± 0.83 (4.79 – 6.98)	−0.659	0.512
Lens volume (mm^3)	230.18 ± 34.27 (173.23 – 290.52)	214.96 ± 40.37 (163.56 – 304.15)	1.601	0.115
RLP	0.2064 ± 0.0142 (0.1812 – 0.2295)	0.2142 ± 0.0083 (0.2008 – 0.230)	−2.439	0.019

CLT:Central lens thickness, PLT:peripheral lens thickness, RCALS:radii of curvature of anterior lens surface, RCPLS:radii of curvature of posterior lens surface, RLP: relative lens position

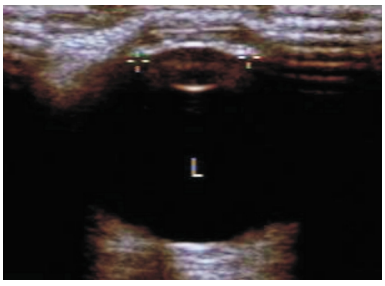

Fig 1 B-ultrasound photograph of normal eye, showing normal lens thickness and flat curvature of anterior lens surface(male, 64 years old)

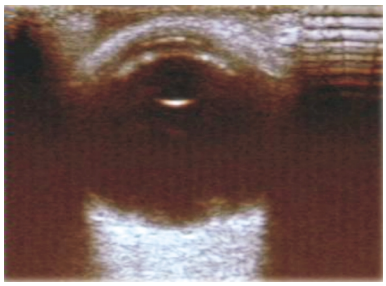

Fig 2 B-ultrasound photograph of PACG, showing increased lens thickness and steeper curvature of anterior lens surface(male, 65 years old)

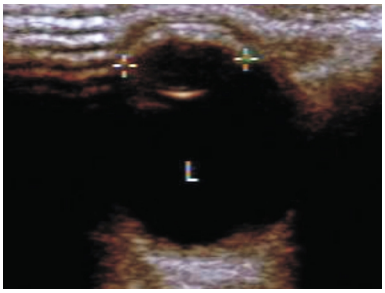

Fig 3 B-ultrasound photograph of normal eye, showing normal lens thickness and flat curvature of anterior lens surface(female, 76 years old)

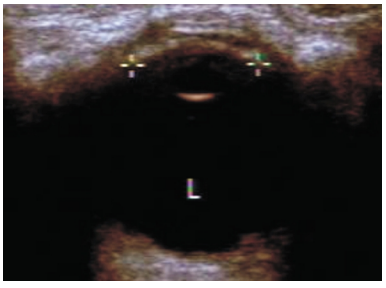

Fig 4 B-ultrasound photograph of PACG, showing increased lens thickness and steeper curvature of anterior lens surface(female, 76 years old)

Comparison of other anterior segment parameters between PACG eyes and control eyes

The anterior chamber depth(ACD), angle opening distance (AOD_{500}) and trabecular iris angle(TIA) of the PACG group were smaller than those of normal control group, and the differences were significant ($P < 0.001$). The PACG group had a significantly smaller trabecular ciliary processes distance(TCPD) than control group($P < 0.05$)(***Tab 2***,***Fig 5***,***6***,***7 and 8***)

Correlation analysis between the radii of curvature of anterior lens surface and other parameters of anterior segment in two groups

In both PACG and control groups, the RCALS had a significantly negative correlation with the central and peripheral lens thickness ($P < 0.01$ and $P < 0.05$ respectively), and had positive correlation with relative lens position(RLP), anterior chamber depth (ACD), angle-open distance at 500 μm(AOD500), trabecular iris angle(TIA) and trabecular ciliary processes distance(TCPD)($P < 0.05$ or $P < 0.01$, ***Tab 3***)

Tab 2 **Comparison of other anterior segment parameters between two groups** ($\bar{x} \pm s$)

parameters	PACG group ($n = 38$)	Control group ($n = 35$)	T value	P value
ACD(μm)	1850.97 ± 293.96 (1381–2639)	2269.77 ± 274.31 (1766–2722)	–5.705	0.000
AOD500(μm)	102.71 ± 92.42 (0–347.5)	239.80 ± 86.88 (104.5–444)	–5.920	0.000
TIA (°)	11.33 ± 9.97 (0–40.44)	24.99 ± 7.42 (10.4–40.29)	–6.019	0.000
TCPD(μm)	771.23 ± 149.59 (459–1105.5)	868.28 ± 194.96 (414.5–1207.5)	–2.163	0.035

ACD: anterior chamber depth, AOD_{500}: angle opening distance at 500 μm, TIA: trabecular iris angle, TCPD: trabecular ciliary processes distance

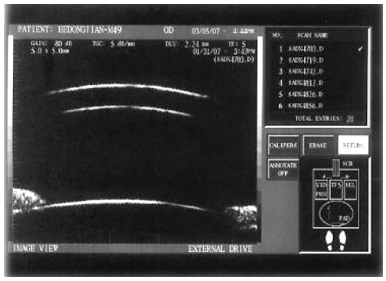

Fig 5 UBM photograph of normal eye, showing normal anterior chamber depth.

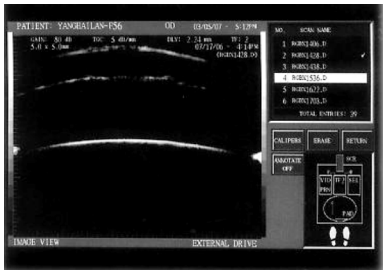

Fig 6 UBM photograph of PACG, showing shallower anterior chamber depth.

Fig 7 UBM photograph of normal eye, showing normal AOD_{500}, TIA and TCPD.

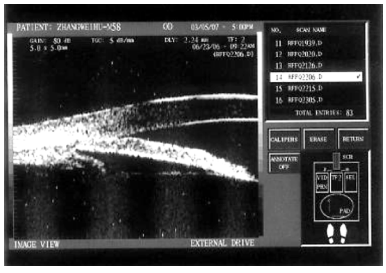

Fig 8 UBM photograph of PACG, showing narrower AOD_{500}, smaller TIA and shorter TCPD.

Tab 3 **Pearson Correlation between the radii of curvature of anterior lens surface and other parameters of anterior segment in two groups**

	CLT	PLT	RLP	ACD	AOD500	TIA	TCPD
RCALS of PACG group	–0.471**	–0.405*	0.389*	0.688**	0.561**	0.563**	0.621**
RCALS of control group	–0.497**	–0.378*	0.405*	0.459*	0.615**	0.578**	0.540**

*$P < 0.05$, **$P < 0.01$

DISCUSSION

Previous research has confirmed that many anatomical factors of anterior segment predispose themselves to the development of PACG, such as microcornea, shallower anterior chamber, increased lens thickness, more anterior position of the lens, shorter axial lengths, hypertrophy of the ciliary body and iris root, more anterior position of ciliary processes and the attachment point of the iris root, etc. In this study, we compared the parameters of PACG and normal eyes. The results indicated that in the PACG group, the anterior chamber depth (ACD) was 0.42mm shallower than that of control group, the central lens thickness (CLT) was 0.26mm thicker,the relative lens position(RLP) was more anterior, the angle-open distance at 500 μm (AOD_{500}) was 0.137mm smaller, the trabecular iris angle(TIA) was 13.66° narrower, and the trabecular ciliary processes distance (TCPD) was 0.097mm shorter. The present results were consistent with previous reports [1-4,7-9]. It was further confirmed that the PACG eyes trend to have more crowded anterior segment structures, shallower anterior chambers, and the angles were prone to close.

Different from the cornea, the iris and the ciliary body, the shape of lens changes more apparently with aging. The lens subcapsular epithelium cells proliferate and produce lamellar fibers continuously, so that the lens gradually becomes larger and thicker. Strenk *et al* [10] investigated the effect of age on the human lens cross-sectional area by magnetic resonance imaging ,suggesting that lens growth is confined to the anterior portion. Leonard *et al*[11] demonstrated that the rate of anterior lens growth was about 0.0385 mm per year (assuming linear anterior growth of the lens). The increased lens thickness results in a tighter attachment and increased contact area between lens and iris, which exacerbate the physiological pupillary blockage. The physical obstruction of the outflow of aqueous humor from the posterior chamber to the anterior portion through the pupil will increase the intraocular pressure of the posterior chamber, thus pushing the peripheral iris forward, leading to bulged iris towards the anterior chamber. The shallower anterior chamber will cause a narrowed angle which is easy to close. This phenomenon, that with aging the thickness of the lens increases and the position of lens becomes more anterior, can be observed both in PACG and normal eyes. Our measurements showed that the central lens thickness of PACG eyes was larger than that of control eyes at the same age, and the lens was relatively more anteriorly positioned, which intensified the tendency of shallow anterior chamber and the angle to close in PACG. The alteration of the lens shape and position can affect other parameters of anterior segment such as iris configuration, anterior chamber depth, angle width, etc. Pupillary block takes part in the mechanism of angle closure in 92.9% of patients with PACG[12]. So lens factors play an important role in the development of this disease. The increased lens thickness in eyes with PACG has led to trials of lens extraction as primary management for PACG [13-17].

We measured the radius of curvature of anterior lens surface (RCALS) of PACG and normal eyes in this study, the results showed that there was a significant difference in the RCALS between the two groups with the PACG group having smaller RCALS. This was consistent with Lowe's report [18]. Lowe and other investigators [18,19] demonstrated a significant positive correlation of RCALS with axial length and anterior chamber depth, and negative correlation with age and lens thickness in both PACG and normal eyes. Lowe suggested that it was necessary to take into account the relationship of the RCALS and pupillary blockage. Huang *et al*[20] investigated the interaction between aqueous humor and the mobile iris by computer simulation and concluded that, greater lens curvature and more anterior lens position contribute significantly to pupillary blockage and to the associated narrowing of the angle. We used Pearson correlation to analyze the relation between the RCALS and other anterior segment parameters in the two groups. The results indicated that both RCALS of PACG and control groups had significantly negative correlation with the central and peripheral lens thickness, and had positive correlation with relative lens position (RLP), anterior chamber depth(ACD), angle-open distance at 500 um (AOD_{500}), trabecular iris angle(TIA) and trabecular ciliary processes distance (TCPD). This indicated that the steeper curvature of anterior lens surface, the thicker lens and the more anterior lens position and the more serious occlusion of the pupil and the shallower anterior chamber and the narrower angle and the more anterior cillary body. This study showed the curvature of anterior lens surface was closely related to the development of PACG. Thus with aging the mutual relationship between increased lens thickness and steeper curvature of anterior lens surface needs to be further researched in the approaching time.

This research analyzed the contributions of peripheral lens thickness (PLT),lens diameter(LD),Lens

volume (LV) and the RCPLS to the development of PACG. The results demonstrated that the PLT of PACG group was 0.22 mm thicker than that of control group, and the difference was statistically significant ($P < 0.05$). This observation suggested that the peripheral lens thickness (PLT) and central lens thickness (CLT) increase in a synchronized pace, with the former being a little slower. This alteration was consistent with the steepness of the curvature of anterior lens surface. The observation showed that the eyes of PACG had larger lens diameter and volume, and smaller RCPLS than the control eyes , but the differences between two groups were not statistically significant ($P > 0.05$), indicating a less importance of these three parameters in the development of PACG. However this implication may need further confirmation with larger sample size in further study.

In conclusion, the abnormal anatomical structure of eyeball was closely related to the development of PACG, particularly the lens shape and position. The thickened lens, steepened curvature of anterior lens surface and more anterior lens position contribute to the papillary blockage and shallower anterior chamber and thus the associated closure of the angle and increased intraocular pressure. Compared to the lens thickness and lens position, Maybe, the curvature of anterior lens surface contributes more significant to the etiology of PACG.

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