

# Obstructive sleep apnea-hypopnea syndrome patients prone to developing anisometropia

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## Research article

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# Abstract

**Objective:** This study aims to investigate anisometropia in obstructive sleep apnea-hypopnea syndrome patients. **Methods:** The obstructive sleep apnea-hypopnea syndrome cohort was divided into groups according to sleeping position: positional obstructive sleep apnea-hypopnea syndrome group (OSA-S group) (n=32), subjects who slept on their sides, and non-positional obstructive sleep apnea-hypopnea syndrome group (OSA-NS group) (n =29), subjects who did not sleep on their sides. The incidence of anisometropia, values of corneal topography, and ocular axial length were compared between groups, and the incidence of anisometropia at different degrees of obstructive sleep apnea-hypopnea syndrome severity was analyzed. **Results:** The obstructive sleep apnea-hypopnea syndrome groups had a significantly higher incidence of anisometropia than the control group. The OSA-S group had a significantly higher incidence of anisometropia compared with the other groups. There was a significant difference in the incidence of anisometropia between the two obstructive sleep apnea-hypopnea syndrome subgroups with different degrees of severity. The obstructive sleep apnea-hypopnea syndrome groups had significantly higher surface regularity index, surface asymmetry index and cylinder values than the control group. In the OSA-S group, the surface regularity index, surface asymmetry index and cylinder of the eye on the preferred sleeping side were significantly higher than those in the contralateral eye. The ocular axial length of the eye was significantly greater on the preferred sleeping side than in the contralateral eye in the 22 patients with anisometropia in the OSA-S group ( $P<0.05$ ). **Conclusions:** obstructive sleep apnea-hypopnea syndrome patients who usually sleep on one side are prone to developing anisometropia, and the incidence of anisometropia is associated with the severity of obstructive sleep apnea-hypopnea syndrome.

## Background

Anisometropia is a condition in which spherocylindrical refractive error differs between the right and left eyes, which can lead to Amblyopia and strabismus [1]. It is an ophthalmology common disease. Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a chronic syndrome characterized by recurrent apnea and/or hypopnea during sleep. Upper airway stenosis causes hypoxemia and hypercapnia, which can lead to multiple organ dysfunction [2], and is associated with systemic diseases, such as hypertension, diabetes and coronary arteriosclerosis [3], and changes in the eyes include floppy eyelid syndrome, keratoconus and glaucoma [4-6]. The degree of eyelid laxity is different between the two eyelids in OSAHS patients who slept on one side, with the ipsilateral eye (the eye on the preferred sleeping side) having a more severe eyelid laxity, compared with the contralateral eye [7]. In the clinic, we also noticed that these patients often had anisometropia, and the ipsilateral eye had a significantly higher myopic degree than the contralateral eye. The causes of different degrees of laxity between these two eyelids mainly due to matrix metalloproteinases in elastic fiber degradation [8,9], however it is unknown if the sleeping position alters anisometropia. This study investigates the association between sleeping position and anisometropia in patients with OSAHS.

## Methods

# Subjects

This study was performed at the Second-affiliated Hospital, Fujian Medical University, (People's Republic of China), and was approved by the Institutional Review Board. A total of 61 patients (122 eyes) diagnosed with OSAHS were enrolled between September 2012 and March 2013 from the Department of Respiratory Medicine of The Second Affiliated Hospital of Fujian Medical University. These patients each had an Apnea-Hypopnea Index (AHI) of  $\geq 5$ . Among these enrolled patients, 41 patients (67.2%) were male and 20 (32.8%) patients were female, and the mean age was  $36.57 \pm 11.27$  years old. Another 67 healthy subjects (134 eyes) from the Physical Examination Center of the same hospital were recruited as the control group. These subjects did not present with obesity, snoring, or allergic rhinitis. The control group comprised of 38 male and 29 female subjects, and the mean age of these subjects was  $37.27 \pm 10.55$  years old. No significant difference was found in age or gender between the OSAHS group and control group ( $t = 1.03$ ,  $P > 0.05$ ;  $\chi^2 = 1.16$ ,  $P > 0.05$ ). Furthermore, no patient had an eye diseases (such as pterygium, corneal scarring, xerophthalmia, keratitis, cataract, glaucoma, or fundus lesions) that can alter diopter. None of the patients studied had a history of ocular trauma or surgery.

## Methodology

The general information and medical history of all subjects were collected. OSAHS patients were divided into three groups according to their AHI scores: mild ( $5 \leq \text{AHI} \leq 15$ ,  $n = 10$ ), moderate ( $15 < \text{AHI} \leq 30$ ,  $n = 19$ ) and severe OSAHS ( $\text{AHI} > 30$ ,  $n = 32$ ). The OSAHS group was further divided into two groups: positional OSAHS group for patients who slept on their sides (OSA-S group); non-positional OSAHS group (OSA-NS group) for patients who did not sleep on their sides. Similarly, the control group was also divided into the positional control group (Nor-S group) and non-positional control group (Nor-NS group) (Figure 1). The positional group was defined as subjects who received more than seven hours of sleep a night and slept on the same side more times. The non-positional group was defined as subjects who received more than seven hours of sleep, and sleep on their backs or alternate sides at night.

All subjects underwent corneal topography using a topographer (SW-6000, Tianjin, China), which was operated by the same person. Three high-quality images were taken. The clearest image, without interference from tears or eyelids, was used to analyze and record the following: corneal surface regularity index (SRI), corneal surface asymmetry index (SAI), cylinder (CYL), flat ( $K_1$ ) and steep ( $K_2$ ), keratometric power, and K ( $[(K_1 + K_2)/2]$ ).

The ocular axial length was measured five times using optical coherence interferometry (Lenstar LS900, Switzerland) to obtain the mean value for all subjects.

All subjects underwent optometry after mydriasis using tropicamide eye drops once every 10 minutes (one drop per eye each time, five times). The spherical degree, cylinder degree and cylinder axis were recorded after successful mydriasis, using an automatic refractometer (Topcon, RM8900, Japan). The patient was diagnosed with anisometropia when the difference in spherical degree between two eyes was greater than or equal to 1.00 D, or when the difference in cylinder degree was greater than or equal to 0.75 D [1].

## Statistical analysis

Statistical analysis was performed using SPSS 17.0. Continuous variables were expressed as  $\pm$  standard deviation (SD). A unpaired t-test was used to compare normally distributed continuous variables between groups, and a Wilcoxon rank-sum test was used for non-normally distributed continuous variables. Categorical variables were expressed as absolute numbers and percentages, and a comparison between groups was conducted by chi-square test.  $P < 0.05$  was considered statistically significant.

K value refers to the average corneal refractive power, K value can be expressed as refractive myopia, mainly used to distinguish axial or corneal refractive factors caused by anisometropia.

## Results

### Optometry *after mydriasis*

The OSAHS group had a significantly higher incidence of anisometropia, compared with the control group (47.5% [29/61] vs. 16.4% [11/67],  $\chi^2 = 14.40$ ,  $P < 0.05$ ). Where 22 of the 32 patients (68.8%) in the OSA-S group being diagnosed with anisometropia. Moreover, 20 patients in the OSA-S group had a higher myopic degree of the eye on the preferred sleeping side, compared with that of the contralateral eye. There were 7 (24.1%) of anisometropia in the OSA-NS group, 4 (16.7%) in the

**Nor-S group, and seven (16.3%) in the Nor-NS group.**

**A significant difference occurred in the incidence of anisometropia in the four groups ( $\chi^2=31.35$ ,  $P<0.05$ ). Where the OSA-S group had a significantly higher prevalence of anisometropia, compared with the OSA-NS, Nor-S, and Nor-NS groups ( $\chi^2=12.14$ ,  $P<0.05$ ;  $\chi^2=14.96$ ,  $P<0.05$ ;  $\chi^2=21.30$ ,  $P<0.05$ ; respectively). The prevalence of anisometropia in the OSA-NS group was similar to that in the Nor-S or Nor-NS groups ( $\chi^2=0.45$ ,  $P>0.05$ ;  $\chi^2=0.68$ ,  $P>0.05$ ). Furthermore, there were no significant differences in the prevalence of anisometropia in the Nor-S and Nor-NS groups ( $\chi^2=0.002$ ,  $P>0.05$ ). The results are presented in Table 1.**

## **Corneal topography**

The OSAHS group had significantly higher cylinder (CYL), greater surface regularity index (SRI), and increased surface asymmetry index (SAI) values compared with the control group ( $P<0.05$ , Table 2), although there were no significant differences in the K value ( $P>0.05$ ). The CYL, SRI and SAI of the ipsilateral eye on the preferred sleeping side in the OSA-S group were significantly higher than those of the contralateral eye ( $P<0.05$ , Table 3), but the K-value was similar for these measurements ( $P>0.05$ ). Furthermore, there were no differences in SRI, SAI, K, or CYL between the two eyes in the OSA-NS, Nor-NS or Nor-S groups ( $P>0.05$ ).

## **Optical coherence interferometry**

A significant difference in ocular longer axial length was found between the ipsilateral eye on the preferred sleeping side and contralateral eye in the 22 patients with anisometropia in the OSA-S group ( $P<0.05$ , Table 4).

## Comparison of the incidence of anisometropia between the OSAHS subgroups with different degrees of severity

The incidence of anisometropia was significantly different in the OSAHS groups ( $\chi^2=14.25$ ,  $P<0.05$ ). The incidence of anisometropia was similar in the mild and moderate OSAHS groups ( $\chi^2=0.14$ ,  $P>0.05$ ). However, the incidence of anisometropia was greater in patients with severe OSAHS group when compared with those in the mild and moderate OSAHS groups ( $\chi^2=3.95$ ,  $P<0.05$ ;  $\chi^2=6.25$ ,  $P<0.05$ ). The results are presented in Table 5.

## Discussion

It was observed in the clinic that OSAHS patients often had anisometropia, and the ipsilateral eye (the eye on the preferred sleeping side) had a significantly higher myopic degree, compared with the contralateral eye (the other one). The influence of sleeping position on anisometropia has not previously been reported. Therefore, a study was performed on the clinical data of OSAHS patients to investigate the association between sleeping position and anisometropia.

Our study indicates that anisometropia is more prevalent in patients in the OSAHS group. The extent of anisometropia was greater in the OSA-S compared with the Nor-S group, suggesting a role for sleep position. Of the 32 patients in the OSA-S group, 22 (68.8%) had anisometropia, with 20 of these patients having a higher myopic degree of the eye on the preferred sleeping side, compared to the contralateral eye. These findings suggest that OSAHS patients who sleep on one side are prone to developing anisometropia and myopia. Two possible reasons exist for this finding: Firstly, OSAHS is characterized by chronic intermittent hypoxia, which can cause changes in the metabolism, function and morphological structure of the ocular tissues [10,11]. Increased degradation of collagen fibers in the cornea and sclera can alter the morphological structure of the eyeballs. Another consideration is that patients with OSAHS have a lower level of cortical arousal, so that, these do not turn over subconsciously when the eyelids are subjected to high mechanical compression [12]. The combination of these aspects likely increases the development of anisometropia in patients with OSAHS who have a preferred sleeping side.

In 22 of the patients with anisometropia in the OSA-S group, anisometropia was diagnosed in 11 cases due to differences in spherical degree, while diagnosis in the remaining 11 cases was due to differences in cylinder degree. This suggests that OSAHS patients who slept on one side may have different types of

anisometropia due to changes in the morphological structures of the cornea and sclera. The reason for this remains unclear, but could be due to differences in mechanical compression in the eyes during sleep.

The results of the corneal topography revealed that the CYL, SRI and SAI of the eye were greater on the preferred sleeping side in patients in the OSA-S group, while the K value was similar in the ipsilateral and contralateral eyes. Furthermore, no significant differences were found between the ipsilateral and contralateral eyes in terms of the CYL, SRI, SAI and K values in the Nor-S group. These results indicate that differences in spherical degree were not due to changes in the cornea. The CYL, SRI and SAI of the ipsilateral eye were significantly higher than those of the contralateral eye in the OSA-S group, suggesting that compression of the ipsilateral eye may cause changes in the morphological structure of the cornea and increase the degree of corneal astigmatism.

The development of myopia is closely associated with the increased ocular axial length caused by scleral thinning and lengthening, leading to a higher spherical degree [13-19]. The ipsilateral eye had a longer ocular axial length, compared with the contralateral eye in the OSA-S group, suggesting that the increased ocular axial length of the ipsilateral eye is associated with the sleeping position of OSAHS patients, and that the increase in ocular axial length of the ipsilateral eye is in turn is correlated with the difference in spherical degree. Researches has confirmed that OSA is closely related to FES and keratoconus [20,21]. Donnenfeld [22] also noted that FES and keratoconus localized to the side of sleeping preference, and hypothesis that eye rubbing maybe the casual fator in KC and FES. Based on the results of our and others' researches, we boldly speculate that when the ipsilateral eye is subjected to compression, it may cause changes in the morphological structure of the sclera and increase the myopic degree, leading to the development of anisometropia in OSAHS patients. Furthermore, fluid retention plays a major role in OSA [23], recent investigations suggest that some of the fluid retained in the legs during the day may redistribute rostrally when recumbent [24,25]. Therefore, we suspect that liquid may stay in the preferred sleeping side of the eyelid, causing some mechanical stress on the eyeball and anisometropia.

The incidence of anisometropia was associated with the severity of OSAHS in our study.. Patients with severe OSAHS had a significantly higher incidence of anisometropia, compared to patients with mild OSAHS. These data further confirms the association between OSAHS and anisometropia. Patients with severe OSAHS are more prone to developing floppy eyelid syndrome, have a higher degree of laxity, and increased expression of matrix metalloproteinases may be the pathophysiological basis for the higher incidence of anisometropia [7].

The results of two patients in the OSA-S group who had a higher myopic degree in the contralateral eye were not excluded from our analysis. It is possible that these patients incorrectly recalled their sleeping positions, or that these patients had undiagnosed anisometropia before the onset of OSAHS.

Although we have done many works in the research, it still has some limitations. (1) OSHAS patients often have other diseases, such as diabetes, hypertension and obesity, did not completely excluded in the study, which might influence the results. (2) There is no more objective evaluation method for the patient's sleep posture, which may cause certain errors. (3) The relevant data of FES were not collected in

the study, and may have some defects. In the future research, FES related data should be collected, and the relationship between FES and anisometropia should be further studied.

## **Abbreviations**

OSAHS: obstructive sleep apnea-hypopnea syndrome

AHI: Apnea-Hypopnea Index

SRI: surface regularity index

SAI: surface asymmetry index

CYL: cylinder

## **Declarations**

## **Ethics approval and consent to participate**

This study was conducted in accordance with the declaration of Helsinki. This study was approved by the Ethics Committee of The Second Affiliated Hospital of Fujian Medical University. Written informed consent was obtained from all participants.

## **Consent to publish**

We have obtained consent to publish from the participant to report individual patient data (including images), written informed consent for the publication was obtained from the participant.

## **Availability of data and materials**

All data generated or analysed during this study are included in this published article [and its supplementary information files].

## **Competing interests**

None of the authors have any financial disclosure or conflict of interest.

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## Authors' Contributions

HXZ been involved in drafting the manuscript and revising it critically for important intellectual content; YYG made substantial contributions to conception and design of the work; XYC and YMZ made substantial contributions to the acquisition, analysis, and interpretation of data for the work; all authors given final approval of the version to be published.

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## Tables

Table 1 Comparison of the incidence of anisometropia between groups

| Groups (number) | Anisometropia       |    | No anisometropia | Total |
|-----------------|---------------------|----|------------------|-------|
| O-S group       | 22                  | 10 | 32               |       |
| O-NS group      | 7*                  | 22 | 29               |       |
| N-S group       | 4* $\diamond$       | 20 | 24               |       |
| N-NS group      | 7* $\diamond\Delta$ | 36 | 43               |       |

Note: \* compared with the O-S group,  $P < 0.05$ ;  $\diamond$  compared with the O-NS group,  $P > 0.05$ ;  $\Delta$  compared with the N-S group,  $P > 0.05$ .

Table 2 Comparison of the values of corneal topography between the OSAHS group and the control group

| Groups |             |               | <i>t</i> | <i>P</i> |
|--------|-------------|---------------|----------|----------|
|        | OSAHS group | Control group |          |          |
| SRI    | 0.34 ± 0.04 | 0.053 ± 0.01  | 82.65    | < 0.05   |
| SAI    | 0.37 ± 0.16 | 0.13 ± 0.26   | 16.65    | < 0.05   |
| CYL    | 0.87 ± 0.46 | 0.56 ± 0.36   | 5.88     | < 0.05   |
| K      | 43.88 ± 1.2 | 43.74 ± 0.56  | 1.2      | 0.24     |

Note: CYL = K2-K1; K = (K1+K2)/2

Table 3 Comparison of the values of corneal topography between the two eyes in the O-S group

| O-S group |                 |                   | <i>t</i> | <i>P</i> |
|-----------|-----------------|-------------------|----------|----------|
|           | Ipsilateral eye | Contralateral eye |          |          |
| SRI       | 0.40 ± 0.27     | 0.32 ± 0.32       | 10.66    | < 0.05   |
| SAI       | 0.51 ± 0.22     | 0.36 ± 0.12       | 2.65     | < 0.05   |
| CYL       | 1.18 ± 0.50     | 0.82 ± 0.43       | 3.49     | < 0.05   |
| K         | 44.09 ± 1.31    | 43.93 ± 2.65      | 0.51     | 0.61     |

Table 4 Comparison of the ocular axial length between the ipsilateral eye and the contralateral eye in the patients with anisometropia in the O-S group

| Groups            | Case number | Mean rank | Sum of ranks |
|-------------------|-------------|-----------|--------------|
| Ipsilateral eye   | 22          | 22.5      | 472.5        |
| Contralateral eye | 22          | 20.5      | 430.5        |

Table 5 Comparison of the incidence of anisometropia between the OSAHS subgroups with different degrees of severity

| Group          | Anisometropia | No anisometropia |    | Total |
|----------------|---------------|------------------|----|-------|
| Mild OSAHS     | 2* $\Delta$   | 8                | 10 |       |
| Moderate OSAHS | 5*            | 14               | 19 |       |
| Severe OSAHS   | 20            | 12               | 32 |       |

Note: \* Compared with severe OSAHS,  $P < 0.05$ ;  $\Delta$  Compared with moderate OSAHS,  $P > 0.05$ .

Figures



Figure 1

The obstructive sleep apnea-hypopnea syndrome (OSAHS) and control groups were divided according to sleeping position. sleep on right (A1,A2), sleep on left (B1,B2), sleep on back (C1)