Abstract

Backgrounds: The association of glaucoma and OSA has been published in many reports. Previous study by Mojon et al demonstrated that repeated hypoxia may affect the development of ganglion cell loss. However, it remains unclear whether glaucoma is association with OSA. Thus, objective of this study is to determine the association of primary open-angle glaucoma / normal tension glaucoma and obstructive sleep apnea in Thai patients.

Materials and Methods: Eighty-six patients consecutively admitted for polysomnographic evaluation of suspected obstructive sleep apnea were performed complete ophthalmologic examination. The association between glaucoma and OSA was determined by the Chi-square test and Pearson correlation. P-value<0.05 were considered statistically significant.

Results: Forty-four of the eighty-six patients (51.16 %) who had an AHI higher than 10 and were diagnosed with OSA. Eighteen of them had mild OSA, twelve patients had moderated OSA and fourteen patients had severe OSA. The prevalence of glaucoma in normal group was 7.14 % (3/42). The prevalence of glaucoma in patients with OSA was 13.64% (6/44). There was no statistically significant correlation between presence of glaucoma and OSA. (Chi-square=9.67; df=1; p-value=0.325)

Conclusions: This study indicates that there is no statistically significant association between the presence of glaucoma and OSA in Thai patients. Therefore, the screening for glaucoma in patients with OSA might not be necessary unless further data of the relationship is present.

Key words: glaucoma, obstructive sleep apnea, sleep apnea syndrome
บทความข่าวสาร

จากหลายศึกษาพบความสัมพันธ์ระหว่างโรคต้อหินมุมเปดและโรคทางเดินหายใจอุดกั้นขณะนอนหลับ บางการศึกษาเห็นว่าอาจเกิดจากเซลของจอประสาทตาและเส้นประสาทตาขาดออกซิเจนซ้ำๆกันหลายครั้งในช่วงที่เกิดทางเดินหายใจอุดกั้นขณะนอนหลับ แต่มีบางการศึกษาที่พบว่าอาจไม่มีความสัมพันธ์กัน ดังนั้น การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อศึกษาความสัมพันธ์ระหว่างโรคต้อหินมุมเปดและโรคทางเดินหายใจอุดกั้นขณะนอนหลับในผู้ป่วยชาวไทย โดยศึกษาในผู้ป่วยที่สงสัยว่าอาจเป็นโรคทางเดินหายใจอุดกั้นขณะนอนหลับจำนวน 86 คน ซึ่งได้รับการตรวจทางเดินหายใจและตรวจตาอย่างละเอียดเพื่อหาโรคทางเดินหายใจอุดกั้นขณะนอนหลับและโรคต้อหิน จากการศึกษาพบผู้ป่วยทางเดินหายใจอุดกั้นขณะนอนหลับ 51.16%(44/86) โดยวินิจฉัยจากค่าดัชนีการหยุดหายใจมากกว่า 10 เยอะจากนั้นพบความสูญของโรคต้อหินในกลุ่มที่ตรวจไม่พบโรคทางเดินหายใจอุดกั้นขณะนอนหลับ 7.14%(3/42) และความชุกของโรคต้อหินในกลุ่มที่ตรวจพบโรคทางเดินหายใจอุดกั้นขณะนอนหลับ 13.64%(6/44) แต่ไม่พบความสัมพันธ์ระหว่างโรคต้อหินมุมเปดและโรคทางเดินหายใจอุดกั้นขณะนอนหลับ (Chi-square test=0.967; df=1; p=0.325)

โดยสรุป เนื่องจากการศึกษาไม่พบความสัมพันธ์ระหว่างโรคต้อหินมุมเปดและโรคทางเดินหายใจอุดกั้นขณะนอนหลับในชาวไทย ดังนั้นจึงไม่แนะนำให้มีการตรวจคัดกรองโรคต้อหินในผู้ป่วยโรคทางเดินหายใจอุดกั้นขณะนอนหลับ จนกว่าจะมีการศึกษาขึ้นยังเกี่ยวกับความสัมพันธ์ของโรคทั้งสอง

คำสำคัญ: โรคต้อหิน โรคทางเดินหายใจอุดกั้นขณะนอนหลับ
Introduction

Glaucoma is a leading cause of irreversible blindness throughout the world. Yet the etiology of glaucoma remains unclear. Several reports mention the significance of vascular risk factors, particularly in normal tension glaucoma (NTG). Drance et al. reported that NTG is associated with hemodynamic crises and the reduction of diastolic ophthalmodynamometry levels. NTG patients have significantly greater nocturnal blood pressure drops compared to healthy patients and they lack autoregulation of the optic nerve head circulation. Hematologic abnormalities that were reported to be associated with NTG include increase blood, plasma viscosity and hypercoagulability.

Obstructive sleep apnea (OSA) is characterized by recurrent upper airway obstructions during sleep. The cessation of respiration or reduction of the airway during apnea or hypopnea leads to hypoxia and hypercapnia. The combination of hypoxia, hypercapnia, and increase ventilatory effort causes sleep fragmentation and arousal. The repetitive sympathetic activity during arousal from sleep may cause systemic hypertension, cardiac arrhythmias, cerebrovascular accidents, and polycythemia.

The relationship between glaucoma and OSA has been studied in many reports. Mojon et al suggested that repeated hypoxia may affect the development of ganglion cell loss. Two studies by Geyer et al and Girkin et al reported that there was no association between glaucoma and OSA. It is unclear whether glaucoma is associated with OSA. In patients with OSA, the repetitive periods of apnea during sleep cause transient hypoxia and increase vascular resistance. The vascular impairment may compromise the optic nerve head perfusion and may cause glaucomatous optic neuropathy. Thus, the purpose of this study is to determine the association of glaucoma and OSA in Thai patients.

Materials and Methods:

Study designs: The study design was cross-sectional.

Subjects

Eighty-six patients consecutively admitted for polysomnographic evaluation of suspected obstructive sleep apnea at HRH Princess Sirinthron Medical Center, Srinakharinwirot University were performed complete ophthalmologic examinations. The protocol and informed consent forms were approved by the Ethical committee of the Faculty of Medicine, Srinakharinwirot University, Thailand. Forty-four patients were diagnosed with OSA. Forty-two patients were diagnosed with snoring without OSA and it is this group we call the normal group.

Sleep studies

Overnight polysomnography was recorded in a sleep laboratory. Simultaneous measurements of electroencephalography, electromyography, electro-oculography, electrocardiography, nasal and oral airflow, respiratory movements, and oximetry to measure oxygen saturation were performed. OSA was diagnosed as an apnea / hypopnea index (AHI) higher than 10. The AHI was classified to determine the severity of OSA: mild (AHI, 10-19), moderate (AHI, 20-39), and severe (AHI >40).
Ophthalmic examinations

Each patient underwent a complete ophthalmic examination. Eye examinations in all patients were performed by a single glaucoma specialist. The examination included visual acuity, applanation tonometry, gonioscopy, optic disc morphology. Stereoscopic slit-lamp biomicroscopy with a 90 D lens was used to assessed optic disc morphology. Fundus photography was used to evaluated retinal nerve fiber layer, whereas Humphrey Visual Field Analyzer was used to examine visual field. The criteria for diagnosis of primary open-angle glaucoma (POAG), included typical glaucomatous optic neuropathy, glaucomatous visual field defects, open angle, and untreated IOP above 21 mmHg. The criteria for diagnosis of normal tension glaucoma (NTG) was similar that of POAG with the exception of untreated IOP below 22 mmHg.

Results

Eighty-six patients were examined from May 2008 through July 2009. The demographic data of patients grouped according to the OSA grade are shown in Table 1. Forty-four of the eighty-six patients (51.16%) who had an AHI higher than 10 and were diagnosed with OSA. Eighteen of them had mild OSA, twelve patients had moderate OSA and fourteen patients had severe OSA. There were two glaucoma patients in mild OSA group, one glaucoma patients in moderate OSA group and three glaucoma patients in severe OSA group. The Pearson correlation failed to show any correlation between glaucoma and mild, moderate, severe OSA (p-value=0.53, 0.63, 0.61 respectively).

Table 1. Demographic Data of obstructive sleep apnea (OSA) patients.

<table>
<thead>
<tr>
<th>OSA Grading</th>
<th>No.of Patients</th>
<th>Age (yrs.)</th>
<th>Sex (M/F)</th>
<th>AHI</th>
<th>BMI</th>
<th>IOP OD</th>
<th>IOP OS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (AHI&lt;10)</td>
<td>42</td>
<td>52.5</td>
<td>23/19</td>
<td>3.4</td>
<td>24.9</td>
<td>14.0</td>
<td>14.0</td>
<td>0.87</td>
</tr>
<tr>
<td>SD</td>
<td>10.4</td>
<td>2.6</td>
<td>3.6</td>
<td>3.1</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (AHI 10-19)</td>
<td>18</td>
<td>58.4</td>
<td>12/6</td>
<td>14.1</td>
<td>28.1</td>
<td>13.6</td>
<td>13.8</td>
<td>0.53</td>
</tr>
<tr>
<td>SD</td>
<td>11.9</td>
<td>2.8</td>
<td>3.9</td>
<td>4.5</td>
<td>3.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (AHI 20-39)</td>
<td>12</td>
<td>48.0</td>
<td>11/1</td>
<td>30.4</td>
<td>27.3</td>
<td>12.6</td>
<td>12.7</td>
<td>0.63</td>
</tr>
<tr>
<td>SD</td>
<td>7.8</td>
<td>5.6</td>
<td>2.8</td>
<td>1.2</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (AHI &gt;40)</td>
<td>14</td>
<td>49.9</td>
<td>10/4</td>
<td>67.1</td>
<td>29.9</td>
<td>14.1</td>
<td>14.5</td>
<td>0.61</td>
</tr>
<tr>
<td>SD</td>
<td>10.1</td>
<td>21.3</td>
<td>5.5</td>
<td>3.2</td>
<td>3.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All grading of OSA</td>
<td>44</td>
<td>52.9</td>
<td>33/11</td>
<td>35.4</td>
<td>28.5</td>
<td>13.5</td>
<td>13.7</td>
<td>0.57</td>
</tr>
</tbody>
</table>

BMI = body mass index; IOP = intraocular pressure; OD = right eye; OS = left eye; AHI = apnea/hyponea index
The demographic data of glaucoma patients in this study are shown in Table 2. There were both POAG and NTG patients in each degree of OSA. The severity of glaucoma varied in each group. In normal group, three glaucoma patients were found. The prevalence of glaucoma in the normal group was 7.14 % (3/42). The prevalence of glaucoma in patients with OSA was 13.64% (6/44). There was no statistically significant correlation between presence of glaucoma and OSA. (Chi-square=9.67; df=1; p-value=0.325). When further analysis of other correlations were performed a significant positive correlation was found between AHI higher than 10 and male patients (p-value=0.049). Furthermore, the AHI higher than 10 also shows positive correlation with BMI higher than 24.99 (p-value=0.002).

Table 2. Demographic Data of Glaucoma patients.

| Patient No. | OSA grading | AHl | Sex | Age(yrs.) | BMI | Diagnosis | IOP | C:D | glaucoma severity |
|-------------|-------------|-----|-----|==========|-----|-----------|-----|-----|------------------|
| 1           | normal      | 4.8 | M   | 72       | 23.04 | POAG      | 27,26 | 0.9,0.9 | severe          |
| 2           | normal      | 0.9 | M   | 62       | 21.22 | NTG       | 13,12 | 0.9,0.9 | severe          |
| 3           | normal      | 1.0 | M   | 71       | 23.05 | NTG       | 14,11 | 0.9,0.6 | severe          |
| 4           | mild        | 12.1| M   | 56       | 24.12 | POAG      | 28,25 | 0.9,0.8 | severe          |
| 5           | mild        | 15.5| M   | 49       | 31.00 | NTG       | 16,16 | 0.6,0.6 | mild            |
| 6           | moderate    | 34.0| M   | 41       | 29.30 | NTG       | 12,12 | 0.7,0.7 | moderate        |
| 7           | severe      | 71.6| M   | 40       | 29.74 | POAG      | 20,23 | 0.5,0.5 | mild            |
| 8           | severe      | 54.60| M  | 47       | 29.80 | NTG       | 15,18 | 0.7,0.6 | moderate        |
| 9           | severe      | 58.50| M  | 48       | 25.70 | NTG       | 14,14 | 0.5,0.5 | mild            |

POAG = Primary open-angle glaucoma; NTG = Normal-tension glaucoma; M = male; F = female; BMI = body mass index; AHl = apnea/hyponea index; OSA = Obstructive sleep apnea

Discussions:

Obstructive sleep apnea is characterized by repetitive episodes of upper airway occlusion during sleep combined with symptoms. Apnea can last from 10 seconds to 2 minutes and are terminated by arousal reaction. The repetitive sympathetic activation during arousal from sleep may cause spikes in blood pressure which may lead to a loss of the normal diurnal dip in the mean blood pressure. Several proposed pathophysiologic mechanisms may associate between OSA and glaucoma, although most theories have not received adequate scientific testing. These mechanisms include direct hypoxia injury to the optic nerve, and disrupted autoregulation of blood flow from periods of hypotension during apneas.

Studies of patients with OSA have estimated a POAG and NTG prevalence ranging from 2% to 27%, which compares to an expected 2 % in the general population. Many of these studies are limited by the lack of matched controls, use of historical control, and reliable on symptoms, questionnaires, or trend oximetry studies to diagnose OSA. Mojon et al reported an increase prevalence of glaucoma in a population with newly diagnosed OSA of 7.2%. In a recent paper, Bendel et al reported a high prevalence (27%) of glaucoma in patients with OSA that was confirmed OSA with polysomnography.
In this study, although glaucoma was found in the patients with OSA higher than the normal group (13.64% VS 7.14%), there was no statistical significance (p-value = 0.325). This study was similar to previous studies. The first was published by Geyer et al. and suggested a prevalence of glaucoma of only 2% among 228 patients with OSA, not significantly different from that of the general Caucasian population. The second study by Girkin et al. examined three International Classification of Disease Ninth Revision (ICD 9) diagnostic codes for newly diagnosed glaucoma over 4 year time frame and also searched for sleep apnea diagnoses under a single diagnostic ICD 9 code. They found that the nested case-control study did not support the relationship between glaucoma and OSA.

An elevated IOP is one of the pathophysiologic mechanism, although the cause of glaucoma remains uncertain. Increased IOP is thought to compromise retinal ganglion cell axons and lead to cell degeneration. Other processes may contribute to the death of retinal ganglion cells, including dysfunctional blood flow autoregulation that results in ischemia and hypoxia, oxidative stress with the formation of inflammatory cytokines and free radicals, and aberrant immunity. An elevated IOP is one of the pathophysiologic mechanism, although the cause of glaucoma remains uncertain. Increased IOP is thought to compromise retinal ganglion cell axons and lead to cell degeneration. Other processes may contribute to the death of retinal ganglion cells, including dysfunctional blood flow autoregulation that results in ischemia and hypoxia, oxidative stress with the formation of inflammatory cytokines and free radicals, and aberrant immunity.6,21,22

In patients with OSA, hypoxic ischemia may contribute to optic nerve damage but would not necessarily be expected to do so through the mechanism of rising IOP. This study was found that there was no statistically significant association between AHI and IOP (p-value=0.96). This observation was supported by the results of Geyer et al. which did not find correlation between the two parameters. However, the paper suggested an association between the BMI and OSA but not with glaucoma. Likewise, this study was found a statistically significant correlation between BMI and OSA (p-value=0.002) but not with glaucoma (p-value=0.579).

In this study, the study population was not a random population of patients having OSA but the sample consisted of those who had been referred for polysomnography because they were suspected of having OSA. Therefore, the sample of patients used in this one-year study reflected the population of all patients diagnosed with OSA living close to HRH Princess Sirinthron Medical center during that time. This study demonstrated that the prevalence of glaucoma in OSA patients was higher than in the general population (13.64% VS 2%). Because this study was performed in a specialty clinic, it may have introduced a selection bias from referral mechanism. This study could concluded only that there was no statistically significant correlation between presence of glaucoma and OSA. The data did not allow any conclusion about a direct causal relationship between glaucoma and OSA. In particular, we could not exclude a third factor influencing both glaucoma and OSA.

Conclusion

this study indicates that there is no statistically significant association between the presence of glaucoma and OSA in Thai patients. Therefore, the screening for glaucoma in patients with OSA might not be necessary unless further data of the relationship is present.

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