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Thickness alterations of retinal nerve fiber layer in children with sleep-disordered breathing due to adenotonsillar hypertrophy

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ABSTRACT

Objective: This study is designed to assess whether hypoxia which is caused by apnea and hypopnea episodes, has an effect on retinal nerve fiber layer (RNFL) thickness, using optical coherence tomography (OCT) in pediatric patients with Adenotonsillar hypertrophy (ATH).
Methods: Fifty-seven children patient with AHT, and 31 healthy non-AHT children (between 6 and 12 ages) were enrolled in this study. Obstructive symptoms of the patients with ATH were assessed by using OSA-18 survey. The patients were divided into 2 groups as mild (>60 and <80) and severe (>80) OSAS patients, according to OSA-18 survey total scores. RNFL thickness, in the four quadrants (superior, nasal, inferior and temporal) patient's both eyes, was measured by optical coherence tomography. RNFL parameters of control and patient groups were compared. Correlation between OSA survey scores and RNFL thickness of the patient groups were examined.
Results: A positive correlation was found between ages and RNLF thickness of all subjects enrolled in this study ($r = +0.107$, $p < 0.05$). And also a poor correlation was found between OSA-18 survey scores and RNFL parameters in patient group (between -0.031 and $+0.016$ at right and left eyes, $p > 0.05$). No statistically significant alteration in RNFL thickness was found between the patient and control groups ($p > 0.05$).
Conclusion: Age range (6–12) of the patients with ATH in our study considers that possible OSAS time was not long enough to affect RNLF thickness. Remembering the risk of optic injury development in children with ATH (in a long term), tonsillectomy and/or adenoidectomy operations shouldn't be delayed.

1. Introduction

Sleep-disordered breathing (SDB) is a clinical condition related to increased upper airway resistance and ranges from simple snoring to obstructive sleep apnea syndrome (OSAS) [1,2]. Complex factors such as anatomy, neuromuscular and genetic predispositions play role in etiology, therefore it is multifactorial [1,2]. SDB is commonly seen in pediatric patients. Reported prevalence of snoring and OSAS are 12% and 1–3%, respectively [1]. Adenotonsillar hypertrophy (ATH), which leads to obstruction in upper airway, is the most common cause of OSAS and adenotonsillectomy is curative in most patients [3]. Symptoms seen in SDB comprises, oral breathing, sleep apnea, restless sleep, frequent awakening, hard to breath, snoring and daytime neurobehavioral problems [1–3]. Cognitional, behavioral, cardiovascular and metabolic disorders are the most frequent complications of SDB [1,2]. In addition to this, OSAS, which is the severe form of SDB, has an association with ophthalmic disorders such as floppy eyelid syndrome, visual field defects, retinal vein occlusion, central serous chorioretinopathy, optic nerve dysfunctions and glaucoma in adult patient groups [4–6].

In recent years, despite many studies conducted on the link between OSAS and glaucoma, which is a disease characterized by progressive optic nerve damage, researchers could not reach a consensus on outcomes. Some studies reported high glaucoma prevalence and a decrease in retinal nerve fiber layer (RNFL) thickness in OSAS patients and some other studies reported the exact opposite [6–11]. Suggested pathogenesis of the link is that hypoxia, hypercapnia and increased sympathetic activity resulted from intermittent apnea–hypopnea episodes in OSAS patients,

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start a process leading to optical nerve damage, causing vasospasms, changes in serum nitric oxide level and increased intracranial pressure [12,13].

Optic neuropathy which is a characteristic sign of glaucoma, refers to a pathologic condition characterized by an increase in size of optic nerve head cup/disc ratio and a decrease in RNFL thickness. Alteration of RNFL thickness is an indicator for early glaucoma, therefore detection of RNFL thickness alteration is important in early diagnosis of glaucoma [14]. Optical coherence tomography (OCT) is a non invasive imaging procedure, which enables to interpret cross-sectional imaging of the retinal nerve fiber layer (RNFL), optic nerve head topography and macular thickness in high resolution, thus it provides early diagnosis of glaucoma [15]. Many studies assessing RFNL thickness of OSAS patients as well selected OCT [8–10].

Accepted gold standard for OSAS diagnosis is nocturnal polysomnography [16], however, because it is an expensive and time taking technique, alternative methods were developed especially for ATH patients. OSA-18 survey (tested, reliable and ratified) is one of these methods [17]. The survey was developed for screening pediatric patients with OSAS caused by adenotonsillar hypertrophy [18,19]. OSA-18 survey has a high precision, reliability and responsiveness for OSA syndrome.

In this study, we aimed to investigate whether RNFL thickness values of pediatric patients with severe ATH, which is often seen with OSAS, are affected as in adult OSAS patients.

2. Methods

2.1. Subjects

Subjects enrolled in this study were selected from prepubertal, non-obese, 6–12 aged patients having obstructive complaints such as snoring, mouth breathing and pausing of breathe during sleep for last 2 years. Informed consent was obtained from all parents. This study was approved by institute ethics committee.

All subjects went through an extensive otolaryngologic examination. Using nasal endoscopy, adenoid hypertrophy levels were graded into 4 classes according to Cassano et al. criteria [20]. Adenoid hypertrophy causing airway obstruction classified into Grade-1 25%, Grade-2 25–50%, Grade-3 50–75%, Grade-4 75–100%. Tonsillar hypertrophy was graded using Brodsky scale [21]. Grade 1, tonsils are located at tonsillar fossa and seen hardly behind anterior pillar. Grade 2, tonsils are seen easily behind anterior pillars. Grade 3, tonsils are extended three-quarters of the way to the midline. Grade 4, tonsils obstruct airway totally. Patients with grade 3 and 4 adenoid and/or tonsillar hypertrophy were considered severe ATH and included in the study.

Patients with grade 1–2 ATH, head and neck malformation, and chronic disease were excluded from the study. Ophthalmologic examination was performed for all patients. The patients with ophthalmic surgery history, uveitis, glaucoma, cornea pathology and the patients using contact lenses were not included in the study. The patient group consists of 57 children with grade 3–4 ATH (left and right eyes, total 114 eyes) and the control group consists of 31 children without upper and lower respiratory tract infection, airway obstruction and AHT (left and right eyes, total 62 eyes). Parents of the patients who have severe grade 3–4 AHT were asked to complete the OSA-18 quality of life survey. The survey involves in 18 items in 5 domains of sleep disturbance, physical suffering, emotional distress, daytime problems, and caregiver concerns. A point scale was used ranging from 1 to 7 to assess the severity of the symptoms related in each item. The total score, ranging from 18 to 126, were recorded and were classified as mild (<60); moderate (>60, <80), or severe (>80) in patient group [17].

2.2. Ophthalmologic examination

All subjects underwent autorefractometer and Goldman applanation tonometer examination. Visual acuity and intraocular pressure of all subjects were measured. Anterior segments (using biomicroscopy) and posterior segments (with +90 D noncontact lens) were evaluated. Standard ophthalmologic examinations were performed, including those mentioned above. Spectral domain optical coherence tomography device (RTVue version 4.0; Optovue, Optovue, Fremont, CA) was used for RNFL thickness measurement (Fig. 1). Optical coherence tomography (OCT) that view taking biological tissue layers micron-level high resolution tomographic sections is a new medical imaging-diagnosis method. OCT is used for imaging of anterior segment structures and evaluation of thickness retinal nerve fiber layer as well as macular edema, macular hole, epiretinal membrane, age related macular degeneration. OCT measurements were taken by the same user without making pupil dilation. The RNFL scan pattern completes four circular scans in 0.15 s at a diameter of 3.45 mm, targeted around the optic nerve head. Between the hours of 8:30–9:30 am, all measurements were taken by the same person in compliance with "Fast RNFL protocol" and 3 samples were taken for each eye. Signals stronger than 7 were used for analysis. RNFL thickness measurements of 4 quadrants (superior, nasal, inferior and temporal) and mean RNFL thickness were saved as "micron".

2.3. Statistical analysis

All collected data were tabulated in a spreadsheet using Microsoft Excel for Windows, software version 2003 (Microsoft Corp., Seattle, WA, USA). All analyses were conducted using IBM SPSS statistical software, version 20 (SPSS Inc. Chicago IL, USA). Subjects were divided into three groups: those without ATH, those with moderate (60< OSA-18 survey scoring <80) and severe (OSA-18 survey scoring >80) disease. Data from the three groups were compared using one-way ANOVA for continuous data, and Fisher's exact test for categorical data, when appropriate. Duncan's multiple comparison procedure was employed for pairwise comparisons. The correlation (r) between OSA-18 survey variables and ophthalmologic variables in the moderate/severe OSAS group was evaluated using Pearson's correlation coefficient. A p value less than 0.05 was considered to be statistically significant.

3. Results

The patients were divided into 2 groups according to OSA-18 survey test scores: First group (scores between 60 and 80; moderate OSAS) consisted of 15 patients (mean age; 8.13 ± 1.6 years, body mass index; 19.43 ± 2.11) and second group (over 80; severe OSAS) consisted of 42 patients (mean ages; 8.6 ± 2.1 years, body mass index; 20.93 ± 5.71). No patient had a score less than 60 (mild OSAS) according to OSA-18 survey. Control group consisted of 31 subjects (mean age; 8.59 ± 2.0 years, body mass index; 20.11 ± 2.71). No statistically significant difference could be found between 3 study groups ($p > 0.05$) (Table 1).

The results of Pearson's correlation analysis between the OSA-18 survey score and OCT parameters in all patients revealed a very poor correlation between −0.031 and +0.016 at right and left eyes ($p > 0.05$). OCT measurement regions (superior, inferior, nasal and temporal) were not different in terms of negative and positive correlation distribution. For all subjects, a positive correlation was