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MAIN ARTICLE

Choroidal thickness evaluation in paediatric patients with adenotonsillar hypertrophy

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Abstract

Objective: To investigate choroidal thickness using enhanced-depth imaging optical coherence tomography in paediatric patients with adenotonsillar hypertrophy, with comparison to healthy children, three months after adenotonsillectomy.

Methods: The patients were assigned to three groups: an adenotonsillar hypertrophy group, an adenotonsillectomy group and a healthy control group. In all groups, subfoveal, temporal and nasal choroidal thickness measurements were taken.

Results: In the subfoveal, temporal and nasal regions, choroidal tissue was found to be significantly thinner in adenotonsillar hypertrophy children than healthy children ($p = 0.012$, $p = 0.027$ and $p = 0.020$). The subfoveal and temporal choroidal thickness measurements of adenotonsillar hypertrophy group cases were significantly decreased compared to those in the adenotonsillectomy group ($p = 0.038$ and $p = 0.048$).

Conclusion: There was a significant association between decreased choroidal thickness and adenotonsillar hypertrophy. Adenotonsillar hypertrophy may play an important role in decreased choroidal thickness.

Key words: Children; Choroid; Adenoids; Palatine Tonsil; Tonsillectomy; Optical Coherence Tomography

Introduction

Obstructive sleep apnoea syndrome (OSAS) in children is a serious condition, estimated to occur in approximately 2 per cent of children.[1] Adenotonsillar hypertrophy is considered to be the most common cause of upper airway obstruction in children.[2] Previously, the most common indication for adenotonsillectomy was chronic or recurrent infection; currently, the leading indications for surgery are airway obstruction and sleep apnoea due to adenotonsillar hypertrophy.[3] Recurrent airway obstruction during sleep causes hypoxia, hypercapnia and intra-thoracic pressure changes that affect autonomic, haemodynamic, humoral and neuroendocrine regulation.[4] These changes may influence optic nerve head perfusion and ocular blood flow.

The choroid is one of the most vascularised tissues in the human body, and it assumes important roles in: the oxygenation and nutrition of the outer retina, the temperature regulation of the retina, the positional condition of the retina, and the secretion of growth factors.[5] The choroid is prone to suffer from microvascular atherosclerotic changes and changes inherent to other microvascular systems.[6]

With the development of optical coherence tomography in recent years, it has become possible to display *in vivo* cross-sectional images of the choroid; this technique is referred to as enhanced-depth imaging optical coherence tomography.[7]

Decreased choroidal thickness has been described in high myopia, retinal dystrophy and age-related choroidal atrophy cases.[8–11] Recently, several studies have reported that OSAS patients had decreased choroidal thickness.[12–14] However, the degree to which choroidal thickness and obstructive sleep apnoea (OSA) severity are correlated is not known. In this study, we expected to find a choroidal thickness decrease in paediatric patients with adenotonsillar hypertrophy, with this decrease being a major cause of OSAS at these ages.

We aimed to investigate the effect of adenotonsillar hypertrophy on choroidal thickness, and to compare choroidal thickness in paediatric patients with adenotonsillar hypertrophy with healthy children and three months after adenotonsillectomy.

Materials and methods

This prospective study was approved by the local ethical board for clinical research at a tertiary referral centre. Written informed consent was obtained from all patients and/or their parents. The study included a

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total of 60 consecutive children (29 paediatric patients with adenotonsillar hypertrophy, 18 paediatric patients in the adenotonsillar hypertrophy group who had undergone adenotonsillectomy with at least 3 months' follow up, and 31 healthy control children) who presented to the otorhinolaryngology and ophthalmology out-patient clinics from January to July 2016.

Exclusion criteria included: the presence of systemic diseases; myopia or hypermetropia of more than 3 dioptres; glaucoma; retinal diseases; uveitis; other ocular disturbances such as a cataract that prevent a detailed fundus examination or ocular tests; medical history of ocular surgery; previous injection or laser treatment; or poor image quality associated with unstable fixation. Patients on corticosteroids treatment were also excluded from the study.

Cases were divided into three different groups: an adenotonsillar hypertrophy group, an adenotonsillectomy group and a healthy control group.

The adenotonsillar hypertrophy group comprised 29 paediatric patients with adenotonsillar hypertrophy (12 males and 17 females; average age ± standard deviation (SD) = 7.1 ± 2.4 years (range, 3–14 years)), who suffered from nasal congestion, snoring and open mouth sleeping. They were examined with a flexible fibre-optic endoscope and the dimensions of the adenoids were measured. The tonsils and adenoid tissues of all patients with more than 50 per cent obstruction of the nasopharyngeal airway were diagnosed with adenotonsillar hypertrophy according to the scale described by Brodsky *et al.*[15] All patients in this group underwent adenotonsillectomy.

The adenotonsillectomy group consisted of 18 patients from the adenotonsillar hypertrophy group (8 males and 10 females; average age ± SD = 7.5 ± 2.6 years (range, 3–14 years)), who had undergone adenotonsillectomy with at least 3 months' follow up. Choroidal thickness was measured three months after adenotonsillectomy surgery.

The control group comprised 31 healthy children of similar age and gender (16 males and 15 females; average age ± SD = 8.0 ± 2.0 years (range, 4–11 years)), who did not have any history of adenotonsillar hypertrophy.

Ophthalmic examinations

Choroidal thickness was measured without pupil dilation using Spectralis optical coherence tomography software (version 5.3; Heidelberg Engineering, Heidelberg, Germany). The line scan enhanced-depth imaging mode was used for the 30 measured optical coherence tomography scans. The images were averaged over 100 scans using an automatic real-time imaging value of 100 and active eye-tracking features. Choroidal thickness was defined as the distance between the hyper-scattering line of the retinal pigment epithelial cells and that of the inner surface of the sclera. All optical coherence tomography scans were performed by the same operator. Measurements were made of the central foveal segment, and at segments that were 1500 µm temporal and 1500 µm nasal from the centre of the fovea (Figure 1).

Statistical analysis

The NCSS (2007) statistical analysis and graphics application and PASS (2008) statistical software program (NCSS, Kaysville, Utah, USA) were employed to evaluate the study data. In addition to using descriptive statistics (means and SDs) to evaluate the data, the one-sample Kolmogorov–Smirnov test and receiver operating characteristic analysis were used to compare both the quantitative data and the normally distributed parameters between the groups. The significance levels were set at $p < 0.001$ and $p < 0.05$.

Results

The study included 60 patients (32 (53.3 per cent) females and 28 (46.6 per cent) males) who were examined in our clinic. The patients were assigned to 3 groups: an adenotonsillar hypertrophy group, which comprised 29 paediatric patients with adenotonsillar hypertrophy; an adenotonsillectomy group, which included 18 paediatric patients from the adenotonsillar hypertrophy group who had undergone adenotonsillectomy with at least 3 months' follow up; and a control group, which consisted of 31 healthy children of similar age and gender. Independent-samples tests comparing the groups revealed no statistically significant differences in terms of sex ($p = 0.584$), mean age ($p = 0.102$) or body mass index (BMI) ($p = 0.415$) (Table I).

The average subfoveal choroidal thickness was 328.52 ± 48.50 µm in the control group and 296.97 ± 45.30 µm in the adenotonsillar hypertrophy group; this difference was statistically significant ($p = 0.012$) (Table II). There was a statistically significant difference in subfoveal choroidal thickness between the adenotonsillar hypertrophy group (pre-operative) and adenotonsillectomy group (post-operative). The subfoveal choroidal thickness of the adenotonsillar hypertrophy group was significantly decreased compared to that of the adenotonsillectomy group ($p = 0.038$) (Table III).

The average temporal choroidal thickness was 311.84 ± 72.62 µm in the control group and 275.69 ± 47.52 µm in the adenotonsillar hypertrophy group; this difference was statistically significant ($p = 0.027$) (Table II). The temporal choroidal thickness of the adenotonsillar hypertrophy group (pre-operative) was significantly decreased compared to that of the adenotonsillectomy group (post-operative) ($p = 0.048$) (Table III).

The average nasal choroidal thickness was 259.58 ± 47.04 µm in the control group and 228.97 ± 51.96 µm in the adenotonsillar hypertrophy group; this difference was statistically significant ($p = 0.020$) (Table II). There was no statistically significant difference between the nasal choroidal thickness measurements of the adenotonsillar hypertrophy group (pre-operative)

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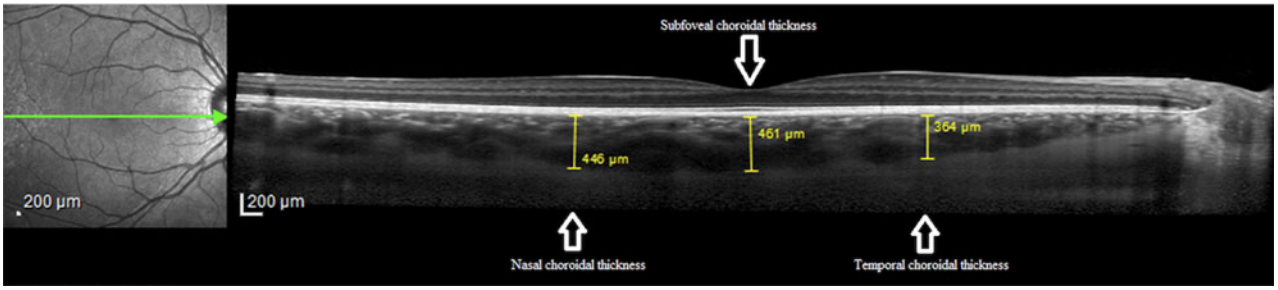

FIG. 1
Measurement of choroidal thickness.

TABLE I
DEMOGRAPHIC DATA

Variable	Adenotonsillar hypertrophy group	Adenotonsillectomy group	Control group	p^*
Sex (*n*)				0.102
– Male	12	8	16	
– Female	17	10	15	
Age (median ± SD (range); years)	7.1 ± 2.4 (3–14)	7.5 ± 2.6 (3–14)	8.0 ± 2.0 (4–11)	0.584
BMI (kg/m^2)	19.2	18.9	19.5	0.415

*Independent-samples test. SD = standard deviation; BMI = body mass index

TABLE II
CHOROIDAL THICKNESS OF ADENOTONSILLAR HYPERTROPHY AND CONTROL GROUPS

Thickness measurement (µm)	Adenotonsillar hypertrophy group	Control group	p^*
Subfoveal choroidal thickness	296.97 ± 45.30	328.52 ± 48.50	0.012†
Temporal choroidal thickness	275.69 ± 47.52	311.84 ± 72.62	0.027†
Nasal choroidal thickness	228.97 ± 51.96	259.58 ± 47.04	0.020†

Data represent means ± standard deviations, unless indicated otherwise. *One-sample Kolmogorov–Smirnov test. †$p < 0.05$

TABLE III
CHOROIDAL THICKNESS OF ADENOTONSILLAR HYPERTROPHY (PRE-OPERATIVE) AND ADENOTONSILLECTOMY (POST-OPERATIVE) GROUPS

Thickness measurement (µm)	Adenotonsillar hypertrophy group	Adenotonsillectomy group	p^*
Subfoveal choroidal thickness	299.87 ± 41.13	317.80 ± 56.92	0.038†
Temporal choroidal thickness	281.27 ± 48.38	305.80 ± 58.42	0.048†
Nasal choroidal thickness	232.33 ± 50.52	243.93 ± 50.93	0.052

Data represent means ± standard deviations, unless indicated otherwise. *Paired samples test. †$p < 0.05$

and the adenotonsillectomy group (post-operative) ($p = 0.052$) (Table III).

Receiver operating characteristic analysis showed that the cut-off values for subfoveal choroidal thickness on admission to predict an OSA in the entire population was 319.0 µm, with a sensitivity of 61.3 per cent and a specificity of 72.4 per cent. The cut-off values for choroidal thickness at the temporal region on admission to predict an OSA in the entire population was 285.5 µm, with a sensitivity of 61.3 per cent and a specificity of 58.6 per cent. The cut-off values for choroidal thickness at the nasal region on admission to predict an OSA in the entire population was 233.5 µm, with a sensitivity of 71.0 per cent and a specificity of 62.1 per cent.

Discussion

Adenotonsillar hypertrophy is the cause of 80 per cent of OSA and respiratory-related sleep disorders in children.[16] Adenotonsillar hypertrophy does not equate to OSA, but it is considered to be the most common cause of upper airway obstruction in children.[2] The number of tonsillectomies performed because of

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infections began to decrease following the availability of more effective antibiotics, together with the more appropriate use of such drugs.[17] The decrease in the frequency of adenotonsillectomies continued until the 1990s, when, with the new emphasis on airway obstruction caused by adenotonsillar hypertrophy, those surgical procedures once again started to escalate.[17] A study noted that, in patients aged 0–3 years, the percentage of adenotonsillectomies performed for obstruction was 92 per cent; this decreased to 73 per cent in 4–10 year olds, and in those aged 11–18 years, surgery rates for obstruction and infection were very similar.[18] Hence, in younger age groups, the main indication for adenotonsillectomy is obstruction. Intermittent airway obstruction in adenotonsillar hypertrophy causes hypoxia and decreases oxygen saturation. Recurrent hypoxia and reperfusion episodes can lead to oxidative stress, inflammation, damaged vascular endothelium and decreased responsiveness to vasodilator agents such as nitric oxide.[19]

- **Obstructive sleep apnoea syndrome (OSAS) in children is a serious condition, affecting approximately 2 per cent of children**
- **Adenotonsillar hypertrophy is the most common cause of upper airway obstruction in children**
- **The choroid is one of the most vascularised tissues and some studies have reported that OSAS patients have decreased choroidal thickness**
- **In this study, choroidal thickness was statistically decreased in paediatric adenotonsillar hypertrophy patients than in healthy children or at three months post-adenotonsillectomy**
- **Reduced choroidal thickening may be used as a biomarker to monitor hypertrophy severity and assess treatment efficacy in children**

Adenotonsillar hypertrophy is one of the most common causes of OSA in children and adolescents. This study included children who snored, were open mouth sleepers, with a hypopnea and apnoea history as in OSA, and who were diagnosed with adenotonsillar hypertrophy because of tonsils and adenoid tissues causing more than 50 per cent obstruction of the nasopharyngeal airway. However, obesity (increased BMI) is another risk factor of similar significance to adenotonsillar hypertrophy. In our study, there was no difference between the BMI of the groups ($p = 0.415$).

The choroid is the vascular layer of the eye that lies between the retina and the sclera. The choroid has an important role in the physiology of the healthy eye and pathogenesis of various ocular diseases.[20,21] Choroidal vessels have fast blood flow and are innervated by a large number of sympathetic nerves.[22] Hypoxia may affect the endothelium and vascular resistance, and further cause structural alterations of the choroid.[23]

In some clinical studies, choroidal thickness was significantly decreased in patients with pathological myopia, age-related macular degeneration, glaucoma and diabetic retinopathy.[24–26] Xin *et al.* found that the severe OSAS group had significantly decreased subfoveal and nasal choroidal thickness than the control, mild and moderate OSAS groups.[12] Using enhanced-depth imaging optical coherence tomography, Kara *et al.* demonstrated that subfoveal choroidal thickness was decreased in patients with moderate or severe OSAS.[13] Karalezli *et al.* reported that the median choroidal thickness was statistically decreased in severe OSAS patients' eyes than in controls' eyes.[14] The authors He and Huang described a significant reduction in subfoveal choroidal thickness in mild, moderate and severe OSAS patients.[27] They also found that four of five studies detected a negative correlation between choroidal thickness on optical coherence tomography and apnoea/hypopnea index. Overall, these studies indicate that choroidal thickness is decreased in OSAS patients.

This study aimed to investigate choroidal structure in paediatric patients with adenotonsillar hypertrophy, using enhanced-depth imaging optical coherence tomography, as decreased choroidal thickness is considered a major cause of OSAS. Choroidal thickness was significantly decreased in paediatric patients with adenotonsillar hypertrophy when compared to measurements of healthy children and at three months after adenotonsillectomy, in the subfoveal, nasal and temporal regions.

Hypoxia and reperfusion episodes cause oxidative stress, inflammation, damage to vascular endothelium, and decreased responsiveness of the vessels to nitric oxide.[19] We think that insufficient vasodilatation of vessels may lead to a decrease in choroidal blood flow. We claim that impaired auto-regulation of the choroid in paediatric patients with adenotonsillar hypertrophy may be responsible for the decreased choroidal thickness compared with that in healthy children and similar to that of OSAS patients.

Choroidal thickness can be easily measured during a routine ophthalmology examination, in 1 minute, within a regular clinic room, and at no extra cost. This measurement can be taken in young children who can communicate. Our study included paediatric patients who were aged three years and over. Our results showed that the choroid was significantly thinner in children with adenotonsillar hypertrophy. However, there are many causes of a thinner choroid. We can use this method with confidence to predict whether children with adenotonsillar hypertrophy will benefit from surgery.

Choroidal tissue takes 85 per cent of the ocular blood flow, and forms the vascular source of the optic nerve head and retinas.[2] Reduced choroidal thickening may be used as a biomarker to monitor hypertrophy severity

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and to assess treatment efficacy in children, rather than assessing ophthalmological problems.

There are several limitations to our study. This was a preliminary study and we did not use polysomnography to confirm that adenotonsillar hypertrophy was causing obstruction in the paediatric patients. Further studies are necessary to examine the correlations between oximetry or polysomnography and sleep-disordered breathing or OSA, and choroidal thickness.

Our method is inexpensive and easy to perform, with good predictive value. We believe this investigation would be suitable for identifying those children with OSA who are likely to benefit from surgical treatment.

Conclusion

Our study revealed that the choroid was significantly thinner in children with adenotonsillar hypertrophy. To the best of our knowledge, this is the first study to demonstrate the relationship between decreased choroidal thickness and adenotonsillar hypertrophy in children. Reduced choroidal thickness may be used as a biomarker to monitor hypertrophy severity and to assess treatment efficacy in children.

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