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Peripapillary retinal nerve fibre layer thickness in women with iron deficiency anaemia

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Abstract

Objective: To evaluate peripapillary retinal nerve fibre layer (RNFL) thickness in adult women with iron deficiency anaemia and healthy control subjects.

Methods: Women with iron deficiency anaemia and age- and sex-matched healthy control subjects were sequentially recruited and underwent detailed ophthalmic examination, including spectral-domain optical coherence tomography (OCT). Serum haemoglobin (Hb), iron and ferritin concentrations, total iron-binding capacity (TIBC) and mean corpuscular volume were determined.

Results: Peripapillary RNFL thicknesses in the nasal and inferior quadrants were significantly smaller in patients ($n = 40$) than in controls ($n = 40$). In the patient group, there were significant correlations between inferior quadrant RNFL thickness and Hb, and between nasal quadrant RNFL thickness and serum iron and ferritin concentrations, and TIBC.

Conclusion: Iron deficiency anaemia reduces RNFL thickness in adult women.

Keywords

Iron deficiency anaemia, adult women, peripapillary retinal nerve fibre layer, spectral-domain optical coherence tomography

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Introduction

Iron deficiency anaemia is the most common form of anaemia, especially in women of childbearing age.[1] Iron is necessary for normal myelination;[2] auditory and visually evoked potentials are reduced due to hypomyelination in patients with iron deficiency.[3] In addition, iron is essential for structural stability and maintenance of the optic nerve.[4] Optical coherence tomography

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(OCT) is a noninvasive imaging method that is widely used in the diagnosis of optic nerve and retinal nerve fibre layer (RNFL) diseases.[5] The spectral domain OCT technique provides faster acquisition, better resolution and improved imaging of retinal morphology than traditional OCT.[6]

In children with thalassaemia major and/or iron deficiency anaemia, OCT studies found that RNFL thicknesses decreased, relative to reduced haemoglobin and ferritin concentrations.[7,8] To the best of our knowledge, RNFL thickness in adult women with iron deficiency anaemia has not been studied. The aim of the present study, therefore, was to evaluate RNFL thickness in adult women with iron deficiency anaemia, and in age- and sex-matched healthy control subjects.

Patients and methods

Study population

The study sequentially recruited women aged 19–54 years who were diagnosed with iron deficiency anaemia at the haematology polyclinic of Recep Tayyip Erdogan University School of Medicine Research and Training Hospital, Rize, Turkey, between May 2014 and July 2014. Iron deficiency anaemia was defined as haemoglobin (Hb) concentrations <12 g/dl and ferritin concentrations <15 mg/l.

Women without iron deficiency anaemia who were attending the Internal Medicine outpatient clinic of Recep Tayyip Erdogan University School of Medicine Research and Training Hospital, Rize, Turkey for routine check-up procedures were recruited as control subjects. Control subjects were required to be free from major disease (including solid cancers, haematological, renal and hepatic diseases and rheumatological disorders).

Exclusion criteria for both patients and control subjects were glaucoma, strabismus, retinal disease, corneal abnormalities, intraocular pressure >21 mmHg in either eye, previous ophthalmic surgery or ocular trauma, age-related macular degeneration, myopia, hyperopia ≥3 diopters, use of steroid or antiglaucoma drugs.

This study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of Recep Tayyip Erdogan University School of Medicine, Rize, Turkey. All participants provided written informed consent before being included in the study.

Ophthalmic examination

A detailed ophthalmic examination (including assessment of refractive error and intraocular pressure, slit-lamp examination, and fundoscopy) was performed for each study participant. All participants underwent peripapillary RNFL thickness measurement via Cirrus® HD spectral-domain OCT (Carl Zeiss Meditec, Dublin, CA, USA). OCT was performed without pupil dilatation and by a single investigator (K.T.). Peripapillary RNFL thicknesses of the temporal, nasal, inferior and superior quadrants, as well as average RNFL thickness, were assessed using an optic disc 200 × 200 cube scan protocol. Cube average thickness (CAT), central subfield thickness (CST) and cube volume (CV) were measured. Scans with signal strength <8 and those during which blinking occurred were excluded from the study.

Laboratory analyses

Full blood count was determined using standard methods and automated haematology analyser (CELL-DYN Ruby; Abbott Laboratories, Abbott Park, IL, USA). Serum iron and iron-binding capacity were evaluated photometrically with an Architect *c*16000 analyser (Abbott Laboratories) and serum ferritin was assessed via chemiluminescent microparticle immunoassay (Architect *i*2000; Abbott Laboratories).

Statistical analyses

Data were presented as mean±SD. Following Kolmogorov–Smirnov testing for normality of distribution, between-group comparisons were made using Student's t-test or Mann–Whitney U-test, as appropriate. Relationships between RNFL thickness and serum haemoglobin, iron and ferritin concentrations, total iron-binding capacity and mean corpuscular volume (MCV) in the patient and control groups were assessed separately using Pearson's correlation coefficient analysis. Statistical analyses were performed using SPSS® version 16 (SPSS Inc., Chicago, IL, USA) for Windows®, and P-values < 0.05 were considered statistically significant.

Results

The study included 40 female patients with iron deficiency anaemia (mean age 38.8 ± 9.2 years; age range 19–54 years) and 40 age- and sex-matched healthy control subjects (mean age 38.2 ± 9.6 years; age range 19–52 years). Clinical characteristics of the patient and control groups are given in Table 1. There were significant between-group differences in haemoglobin, serum iron and ferritin concentrations, MCV and total iron-binding capacity ($P < 0.001$ for each comparison; Table 1).

Data regarding OCT parameters are shown in Table 2. RNFL thickness in both the nasal and the inferior quadrants were significantly thinner in the patient group than in the control group ($P = 0.042$ and $P = 0.047$, respectively). There were no other statistically significant between-group differences.

In the patient group, there were significant positive correlations between inferior RNFL thickness and Hb concentration ($r = 0.221$; $P = 0.049$), and between nasal RNFL thickness and serum iron ($r = 0.263$; $P = 0.018$), total iron-binding capacity ($r = 0.238$; $P = 0.033$) and serum ferritin ($r = 0.284$; $P = 0.011$). There were no other statistically significant correlations in the patient group. There were no statistically significant correlations between RNFL thickness and any parameter in the control group.

Table 1. Clinical characteristics of women with iron deficiency anaemia and healthy age- and sex-matched control subjects included in a study investigating the effect of iron deficiency on peripapillary retinal nerve fibre layer thickness.

Characteristic	Anaemia group $n = 40$	Control group $n = 40$	Statistical significance[a]
Haemoglobin, g/dl	9.4 ± 1.2	12.8 ± 0.6	$P < 0.001$
Mean corpuscular volume, fl	71.8 ± 5.9	87.3 ± 4.6	$P < 0.001$
Serum iron, μg/dl	27.1 ± 16.8	99.7 ± 24.2	$P < 0.001$
Serum ferritin, μg/dl	4.2 ± 3.9	34.8 ± 18.1	$P < 0.001$
Total iron-binding capacity, μg/dl	383.2 ± 49.0	275.1 ± 43.2	$P < 0.001$
Refractive error	1.0 ± 0.8	1.4 ± 0.7	NS
Cup/disc ratio	0.32 ± 0.79	0.29 ± 0.84	NS
Intraocular pressure, mm/Hg	15.8 ± 2.7	14.9 ± 3.0	NS
Signal strength	8.7 ± 0.7	9.1 ± 0.7	NS

Data presented as mean ± SD.
[a]Student's t-test.
NS, not statistically significant ($P \geq 0.05$).

Table 2. Optical coherence tomography parameters of female patients with iron deficiency anaemia and healthy age- and sex-matched control subjects.

Parameter	Anaemia group $n = 40$	Control group $n = 40$	Statistical significance[a]
Peripapillary RNFL thickness, μm			
Superior quadrant	116.4 ± 14.3	117.0 ± 14.0	NS
Nasal quadrant	70.7 ± 10.3	75.3 ± 9.5	$P = 0.042$
Inferior quadrant	120.6 ± 10.9	126.6 ± 15.1	$P = 0.047$
Temporal quadrant	66.7 ± 11.1	67.2 ± 9.2	NS
Mean	93.7 ± 7.7	96.4 ± 8.1	NS
CST, μm	247.3 ± 19.6	241.3 ± 17.2	NS
CV, mm^3	9.2 ± 0.6	9.2 ± 0.7	NS
CAT, μm	277.3 ± 11.1	279.2 ± 7.1	NS

Data presented as mean ± SD.
[a]Student's *t*-test.
RNFL, retinal nerve fibre thickness; NS, not statistically significant ($P \geq 0.05$); CST, central subfield thickness; CV, cube volume; CAT, cube average thickness.

Discussion

The present study found that women with iron deficiency anaemia had significantly smaller RNFL thicknesses in the nasal and inferior quadrants compared with healthy matched subjects. In contrast, children with iron deficiency anaemia have been found to have lower average, superior and inferior RNFL thicknesses compared with controls.[7] A further study evaluating RNFL thicknesses in children with thalassaemia major or iron deficiency anaemia showed that RNFL thicknesses were decreased in all quadrants in children with thalassemia major, but in the inferior quadrant only in children with iron deficiency anemia.[8] The inconsistencies between these studies and our own may be a result of differences in the study populations. It is possible that the continuing development of the nervous system in children may render their nerve fibres more sensitive to changes in serum iron concentrations.

It is well established that iron performs important functions in the central nervous system, including nerve myelination and neurotransmitter synthesis.[9] Oligodendrocytes are crucial for myelination, and iron deficiency adversely affects the normal functioning of these cells.[10] Iron affects myelin synthesis, both directly as a cofactor of cholesterol and lipid biosynthesis and indirectly as an oxidative metabolism component in oligodendrocytes.[11] The high iron and transferrin levels present in newborns underline the importance of iron in the development of the nervous system.[4] RNFL thicknesses in anaemic women were correlated with Hb, iron and ferritin concentrations as well as with total iron-binding capacity in the present study.

The reduced RNFL thickness in patients with anaemia compared with control subjects observed in the present study is likely due to hypomyelination caused by iron deficiency. Iron deficiency is known to play an aetiological role in neurally-mediated syncope and restless leg syndrome.[12,13] Correction of anaemia led to improvements in brain function independent of iron levels in patients with anaemia unrelated to iron deficiency, however.[14,15] The decreased

RNFL thickness in children with thalassaemia major[8] suggests that hypoxia may have contributed to the reductions in RNFL thickness seen in the present study. In patients with sickle-cell disease, vascular occlusions can lead to ischaemic retinopathy, and these patients have thinner peripapillary RNFL than healthy control subjects.[16] This may explain the correlation between ischaemic status and peripapillary RNFL thickness. Iron deficiency anaemia is known to reduce spontaneous blinking rates by triggering dopaminergic dysfunction.[17] Since dopamine is the major retinal neurotransmitter,[18] it would be logical to assume that dopaminergic dysfunction was an additional factor for the RNFL reductions observed in our study.

Malnutrition and deficiencies in trace elements (including iron, zinc and copper) cause detrimental changes in the optic nerve.[4] Trace element status in iron deficiency anaemia is mainly influenced by metabolic interactions between these elements.[19] Decreases in peripapillary RNFL thickness may therefore be influenced by deficiencies in other trace elements besides iron.

The present study has several limitations. The sample size was small and it was not possible to subdivide groups according to severity and duration of anaemia. In addition, we did not re-evaluate peripapillary RNFL thickness after iron supplementation treatment.

The present study shows that iron deficiency anaemia reduces RNFL thickness in adult women. Further studies are necessary to reveal the clinical importance of these findings, and to determine whether these changes could be reversed by treating the anaemia.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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