DOI 10.5935/0034-7280.20150015

Retinal nerve fiber layer in hepatosplenic schistosomiasis mansoni patients: analysis using optical coherence tomography

Camada de fibras nervosas da retina em portadores de esquistossomose mansônica na forma hepatoesplênica: análise por tomografia de coerência óptica

Ana Carolina Celino[1], Carlos Teixeira Brandt[2], Ana Lúcia Maciel[3], Andréa Gondim Leitão Sarmento[3], Laura Santos[4], Neylane Coelho[2], Diego Gadelha[3]

ABSTRACT

Purposes: To evaluate the retinal nerve fiber layer thickness in patients with the hepatosplenic schistosomiasis mansoni using optical coherence tomography . **Methods:** It was performed a observational, analytic, cross-sectional study. The group of patients enrolled 24 individuals (13 females and 11 males), aged from 27 to 73 years (55.7±11.6 years). In the control group were included 22 subjects (12 females and 10 males) aged from 31 to 77 years (55.4±16.5 years). Of the 92 eyes evaluated, three were excluded because they have opaque media, which made impossible to perform the test. All participants underwent a complete ophthalmologic examination and measurement of the retinal nerve fiber layer using optical coherence tomography. **Results:** The mean thickness of retinal nerve fiber layer was 98.1±15.2µm in the studied group and 114.2±10.0 µm in the control group (p<0.001). **Conclusion:** There was a significant decrease in the retinal nerve fiber layer thickness in all quadrants in patients with hepatosplenic schistosomiasis.

Keywords: Schistosomiasis; OCT; Eye; Retinal nerve fiber layer

RESUMO

***Objetivo**: Avaliar a espessura da camada de fibras nervosas da retina em portadores de esquistossomose mansônica na forma hepatoesplênica utilizando a tomografia de coerência óptica. **Métodos**: Realizou-se estudo observacional, analítico, de corte transversal. O grupo de doentes foi composto por 24 indivíduos (13 femininos e 11 masculinos), com idades variando entre 27 e 73 anos (55,7±11,6 anos). No grupo controle foram incluídos 22 indivíduos (12 femininos e 10 masculinos) com idades entre 31 e 77 anos (55,4±16,5 anos). Dos 92 olhos avaliados, três foram excluídos por apresentarem opacidade de meios que impossibilitaram o exame. Todos os participantes foram submetidos ao exame oftalmológico completo e medida da camada de fibras nervosas da retina pela tomografia de coerência óptica. **Resultados**: A média das espessuras da camada de fibras nervosas da retina foi de 98,1±15,2µm no grupo de estudo e 114,2±10,0 µm no grupo controle (p<0,001). **Conclusão**: Observou-se diminuição significante da espessura da camada de fibras nervosas da retina, em todos os quadrantes, nos pacientes com esquistossomose mansônica na forma hepatoesplênica.*

***Descritores**: Esquistossomose mansônica; OCT; Olho; Camada de fibras nervosas da retina*

[1] Federal University of Campina Grande, PB, Brazil.
[2] Federal University of Pernambuco, Recife, PE, Brazil.
[3] Resident in ophthalmology at Fundação Altino Ventura, Recife, PE, Brazil.
[4] Fundação Altino Ventura, Recife, PE, Brazil; Hospital de Olhos de Pernambuco, Recife, PE, Brazil.

Study carried out within the Post-Graduate Program in Surgery of the Federal University of Pernambuco and Fundação Altino Ventura, Recife, PE, Brazil.

The authors declare no conflict of interest.

Received for publication 25/04/2013 - Accepted for publication 24/03/2014

Introduction

Schistosomiasis is one of the most widespread human parasitic infections, constituting a serious world public health problem as it affects approximately 200 million individuals[1-3]..

Mansonic schistosomiasis has the helminth *Schistosoma mansoni* as etiological agent and is endemic in 74 countries, mainly in the eastern Mediterranean, in Africa and in South America[2]. It has been estimated that in Brazil there are approximately ten million infected persons, and Pernambuco is one of the states with most patients, roughly 17% of the population. The disease evolves to serious forms in 3 to 10% of cases[3,4].

The use of praziquantel on a large scale has been pointed out as one of factors responsible for the reduction in serious forms of the disease.However, human prevalence and the establishment of new foci of active parasitosis transmission continue expanding, so that the endemic disease assumes a scale ever more cruel: less lethal, but largely incapacitating, causing physical and moral damage to the affected populations[4,5].

The association between mansonic schistosomiasis, especially in its hepatosplenic form, and ocular lesions has been described. Such lesions occur due to granuloma formation, deposits of antigen-antibody immunocomplexes, and/or direct attack of the larva or the egg to the choroid or retina, which could be harmful, depending on the stricken location[6-11]. Furthermore, in the presence of portal hypertension, a frequent hepatosplenic schistosomiasis complication, there possiblyoccurs a reversal from hepatopetal flow to hepatofugal, through the left gastric vein, influencing azygous system pressure and potentially hindering the drainage of craniofacial structures, and consequently of ocular tissues. This fact was used to justify the description of the delay in the arrival time of fluorescein contrast agent in the early venous phase of the fluorescein angiography examination. It was then suggested that in the retina of schistosomiasis patients there could be arterial irrigation difficulty in the face of capillary pressure increase due to reduced venous drainage of this organ for systemic circulation[11].

The optic nerve and the retina present changing blood flow according to local metabolic needs: this is the autoregulation mechanism[12]. Changes in retinal blood flow that could generate ischemia in this region are involved in damage to the retinal nerve fiber layer, playing a fundamental role in the physiopathology of glaucoma[12,13].

There exists vast documentation on the importance of retinal nerve fiber layer evaluation in the early diagnostic of glaucoma[14-18]. It is believed that structural changes precede functional changes, so that a loss of some 30% or even more of the nerve fiber layer is necessary for detection of functional change by visual field examination[17]..

Optical coherence tomography (OCT) is a recent, non-invasive, non-contact, high-resolution propedeutic technology, which allows the generation of sectional images useful in the diagnostic of several retinal diseases, as well as in the analysis of the nerve fiber layer[14-16,19,20].

Several studies described the effectiveness and reproducibility of this method in the evaluation of the retinal nerve fiber layer (RNFL), in the diagnostic and follow-up of glaucoma[21,22].

The suspicion that portal hypertension can bring about changes in retinal microcirculation with consequent ischemia and damage to the nerve fiber layer, together with nonexistence of studies using OCT in hepatosplenic schistosomiasis, justify this study.

The study's objective was to evaluate the retinal nerve fiber layer in patients afflicted with hepatosplenic schistosomiasis, using OCT.

Methods

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Results

Frequencies of corrected visual acuity (VA) in both groups are presented in Table 1.

Table 1

Distribution of corrected visual acuity frequencies in both groups

	Study group		Control group		
Visual acuity	**N**	**%**	**N**	**%**	**p-Value**
0.7 - 1.0	43	93.5	40	93.0	0.932
0.5 - 0.6	3	6.5	3	7.0	
Total	46	100	43	100	

Chi-square test

The main changes found in the anterior segment were: conjunctival degeneration (pinguecula / pterygium) in 4 eyes (8.6%) in the study group and in 3 eyes (6.9%) in the control group. Incipient cataract was observed in 9 eyes (19.5%) in the study group and in 10 eyes (18.6%) in the control group. There was no difference between the groups with respect to changes in the anterior segment. There was also no difference between the groups with as to the IOP mean, which was 12.1 mm Hg in the study group and 12.4 mm Hg in the control group(p=0.957). The main change found in the posterior segment examination was the vascular tortuosity present in 12 eyes (26.1%) of subjects belonging to the study group and in 5 eyes (11.6%) of those belonging to the control group. Furthermore, we observed atrophy of the retinal pigment epithelium (RPE) in 8 eyes (17.3%) in the study group and in 3 eyes (6.9%) in the control group. There was a statistically significant difference between the groups as to vascular tortuosity (p=0.03).

With respect to the OCT results, it was observed that the study group presented a smaller thickness in the nerve fiber layer compared to the control group, and that this difference was significant in all quadrants (Table 2).

Table 2

Mean thickness distribution of retinal nerve fiber layer in the respective groups

Variables	Groups	N	Variation (μm)	Mean	SD	P
CFN	Study	46	54.7 - 128.2	98.1	15.2	<0.001
Mean*	Control	43	89.1 - 132.0	114.2	10.0	
Superior	Study	46	61.0 - 172.0	123.7	26.8	<0.001
quadrant	Control	43	104.0 - 184.0	152.3	19.0	
Inferior	Study	46	57.0 - 172.0	126.3	20.3	0.001
quadrant	Control	43	83.0 - 174.0	139.9	15.4	
Temporal	Study	46	37.0 - 92.0	62.2	14.4	<0.001
quadrant	Control	43	42.0 - 95.0	74.2	10.4	
Nasal	Study	46	42.0 - 130.0	78.6	21.5	<0.001
quadrant	Control	43	66.0 - 128.0	99.5	16.2	

(*) average of all four quadrants : Student's *t*-test

Discussion

Hepatosplenic schistosomiasis is associated with ocular changes. The study of RNFL using OCT in patients of this disease is original in the literature. Previous studies reported the presence of subhyaloid haemorrhages, superficial retinal haemorrhages, hard exudates, cotton wool spots, ingurgitation and vascular tortuosity[9,23,24]. These findings suggest that the disease can bring about losses in the microcirculatory balance in these patients' retina. The retinal nerve fiber layer, composed of axons of ganglion cells, is particularly sensitive to ischemia. Ischemia, in turn, can generate irreparable damage to these cells, the progression of which can lead to impairment of visual functions[12,13].

With respect to the anterior segment of the eye, no differences between the groups were observed. In a previous study, a higher prevalence was observed of benign conjunctival degenerations (pinguecula / pterygium) in patients suffering from hepatosplenic schistosomiasis, which could be a consequence of changes in the immunological system of those patients, affecting the quantity and quality of T-lymphocytes[25].

Ocular pressure may be responsible for damage to retinal nerve fibers. This damage may occur by direct compression of the fibers in their passage through the lamina cribrosa or by impairment of local microvasculature, with an increase in vascular resistance and consequent ischemia. Most studies consider values lower than 21 mm Hg as normal ocularpressure[26]. We excluded from this study those subjects presenting IOP above 20 mm Hg,

as this could represent a confusing variable, interfering in the studied phenomenon, i.e. it would be much more likely that RNFL changes occurred due to the high IOP rather than due to the presence of hepatosplenic schistosomiasis. There was no difference in IOP means between the two studied groups. These results agree with other studies[24,25,27].

With respect to the findings in the eye's posterior segment, similarly to what was already reported by other authors, a greater prevalence of vascular tortuosity was observed in the patient group[23-25,27]. In a recent study, a correlation was reported between the presence of vascular tortuosity and the increase of blood flow speed in ocular vessels of patients with hepatosplenic schistosomiasis[24]. Funduscopic lesions suggestive of schistosomiasic chorioretinitis as described in the literature were not observed[6]. This is probably due to the fact that such findings occurred in population studies with a large number of subjects.

A significant difference was observed in the mean of RNFL thickness measurements between the two studied groups. Patients with hepatosplenic schistosomiasis presented a reduction in the thickness of this layer in all quadrants. These findings agree with a similar study published previously in which, by the use of [the scanning laser polarimeter]GDx there was a homogeneous reduction in the RNFL in all sectors of the peripapillary region[28]. The values of means obtained in the patient group are also reduced when compared with the normality standard existing in the equipment's data source, and were compatible with glaucoma, according to studies which evaluated knowingly glaucomatous eyes[16].

The death of ganglion retinal cells, the axons of which make up the RNFL, may be caused by impairment of local microvasculature[29]. It is suspected that hemodynamic changes caused by portal hypertension in hepatosplenic schistosomiasis patients may be responsible for retinal microcirculation dysfunction, with consequent ischemia. Findings of vascular tortuosity, hard exudates and cotton wool exudates in the retina of those patients, as found in previous studies, support this theory. At first it was imagined that these changes were the consequence of reduction in the ocular blood flow, based on the finding of increased arrival time of the contrast agent to the retina during fluorescein angiography examination. Schistosomiasis patients would have a similar behavior to that of cirrhotic patients since they present similar hemodynamic characteristics. A delay in cerebral blood flow was observed while studying patients with cirrhosis and portal hypertension, using angiography with technetium. It was assumed that, similarly, schistosomiasis patients could present slow cerebral blood circulation and consequently slow ocular circulation[11]. However, a recent study evaluated hemodynamic parameters of extraocular blood vessels of hepatosplenic schistosomiasis patients using Doppler ultrasonography demonstrated flow speed increase in the central artery and central vein of the retina (a similar phenomenon to that in the spleen, when hyperflow of the splenic artery conditions dilation, tortuosity and increase in splenic vein flow). This increase in ocular vessel flow speed was attributed to the likely inflammatory process of an immune nature present in this disease[24].

It is possible to assume that hyperflow in larger-caliber retinal arteries may, in the long term, cause structural damage in the precapillary arterioles and capillaries together with vascular resistance increase and consequent ischemia. Furthermore, it is possible that excessive production of inflammatory factors and chemical mediators, such as nitric oxide, reaches damaging levels and are also involved in cellular damage. It is known that nitric oxide, an important vasodilator, can present a paradoxical effect at the retinal vascular endothelium which increases damage to nerve cells through production and combination with high-toxicity free radicals[30].

Based on the above, it is possible to suggest that portal hypertension in hepatosplenic schistosomiasis patients may cause reduction of RNFL thickness and that this change, in the long term, may be associated with glaucoma development. This fact takes on great importance when considering that changes in the retinal nerve fiber layer may precede functional changes in visual field and visual acuity[14-18]. However, longitudinal follow-up studies on these patients are required, in order to investigate the relationship of the present findings with corresponding changes in visual field and optic disc, to support this hypothesis.

Conclusion

Analysis of the results allows us to conclude that the thickness of the retinal nerve fiber layer was significantly smaller in the group of hepatosplenic mansonic schistosomiasis patients than in the control goop, both in quadrant mean value and in the individual values for each quadrant.

The findings in this study can be justified by the secondary hemodynamic changes to portal hypertension present in hepatosplenic schistosomiasis with repercussions in ocular microcirculation.

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Corresponding author:
Ana Carolina Celino
Rua Arquilino de Sousa Guimarães, nº 501 – Jardim Tavares
CEP 58103-263 – Campina Grande (PB), Brasil
E mail: carolinacelino1@hotmail.com