da retina, nomeadamente CGRcom seus axónios e camada plexiforme interna.[3] Os valores que encontramos poderão sugerir precisamente dano mais precoce a estas estruturas da retina, uma vez que na região nasal à fóvea se encontra o feixe papilomacular, onde existem em maior número de CGR e seus prolongamentos axonais. Apesar de o ERGmf ser um exame complementar de diagnóstico que pode detectar alterações precoces na retinopatia dos antimaláricos[13], o seu uso encontra-se limitado pelo custo, disponibilidade e necessidade de um centro especializado, em comparação com o SD-OCT, que é uma ferramenta atualmente mais disponível, dando informações da ultra-estrutura retiniana forma rápida e fácil. Noutros trabalhos, também foi demonstrada a capacidade de o SD-OCT demonstrar casos de toxicidade retiniana inicial, pela medição da espessura retiniana.[2,5,10] Os nossos resultados sugerem que o SD-OCT pode detectar o adelgaçamento retiniano em casos de retinopatia precoce da HCQ. Trata-se de um estudo de pequena dimensão, pelo que mais estudos são necessários para conclusões mais definitivas. Novas modalidades de diagnóstico, nomeadamente estudos de segmentação retiniana também serão úteis para um maior entendimento da fisiopatologia da retinopatia dos antimaláricos.

Em conclusão, dado o potencial de perda visual progressiva e insidiosa associada à retinopatia dos antimaláricos, é fundamental que Oftalmologista tenha ferramentas capazes de detectar precocemente o dano à retina. O SD-OCT, exame amplamente disponível e fiável, pode ser uma ferramenta útil na avaliação do dano retiniano precoce dos antimaláricos.

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Artigo Original

Ocular Disease in Children with Type 1 Diabetes

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RESUMO

A prestação de cuidados especializados aos doentes diabéticos, nos países desenvolvidos, tem contribuído para o reduzido número de complicações a nível ocular na idade pediátrica. A eficiência dos exames anuais oftalmológicos nesta faixa etária é atualmente assunto de debate.
Os autores pretendem analisar as alterações a nível ocular nesta população e adequar os resultados à dinâmica de um centro terciário, através do estudo retrospetivo dos processos clínicos dos doentes com diabetes tipo 1 inscritos e seguidos na consulta de Endocrinologia Pediátrica do Centro Hospitalar Lisboa Central entre Janeiro de 2008 e Julho de 2015. Foram avaliadas as características demográficas, a patologia de base e ocular e a referenciação e seguimento destes doentes na consulta de Oftalmologia Pediátrica.
Após análise dos processos clínicos de 304 doentes com diabetes tipo 1, foram incluídos no estudo 110 doentes com referência a consulta de Oftalmologia no sistema informático. Apresentavam idade média de 13,2 ±3.24 anos (4-20 anos), 57 eram do sexo masculino e 53 do sexo feminino. A diabetes tipo 1 foi diagnosticada em média aos 7,5 ±3.0 anos (0,75-13 anos), com tempo de evolução médio de 6 ±3.3 anos (1-14 anos). A média do último valor de hemoglobina A1c era 8,6% ±1.5 (4,9-14,4%). A primeira referenciação à consulta de Oftalmologia foi em média aos 9,4 ±3.1 anos (2-19 anos), sendo que em 55 casos os doentes tinham menos de 10 anos e, desses, 29 foram referenciados no primeiro ano após o diagnóstico (duração média da diabetes 2,0 ±0.7 anos; 0-7 anos). Relativamente aos 55 doentes referenciados com idade igual ou superior a 10 anos, 27 foram referenciados no primeiro ano após o diagnóstico (duração média da diabetes 2,3 ±0.8 anos; 0-9 anos). Quanto à frequência do rastreio, 54 doentes foram reavaliados após 1 ano, 15 após 2 anos, 1 após 3 anos e 1 após 5 anos. Não foi detetado nenhum caso de retinopatia diabética. 28 doentes apresentavam astigmatismo, 12 hipermetropia, 16 miopia, 5 estrabismo, 2 blefaroptose e 1 catarata polar.
A Sociedade Internacional para a Diabetes Pediátrica e Adolescente recomenda o rastreio oftalmológico 2 anos após o diagnóstico de diabetes tipo 1, em doentes acima dos 10 anos, e 5 anos, se em idades inferiores. As diretrizes de 2014 da Academia Americana de Oftalmologia recomendam que o primeiro exame oftalmológico seja realizado 5 anos após o início da doença e repetido anualmente. Um estudo prévio efetuado no Hospital Dona Estefânia, entre 1999 e 2000, por Rodrigues P et al constatou uma baixa incidência de lesões oculares (6.4%) na população estudada, em acordo com os nossos resultados. Estudos mais recentes publicados na literatura são também concordantes e demonstram que a rara incidência de complicações da diabetes até à puberdade poderá justificar novas orientações nos próximos anos.

Palavras-chave
Diabetes Tipo 1, Patologia Ocular, Idade Pediátrica, Rastreio, Retinopatia

ABSTRACT

Specialized care provided to diabetic patients, in developed countries, has contributed to the reduced number of ocular complications in pediatric age. The effectiveness of annual eye examinations in this group is unclear.

The authors intend to determine the prevalence and onset of ocular disease in this population and adapt the results to the dynamics of a tertiary center, based on a retrospective study of type 1 diabetes patients' medical records registered and monitored in Pediatric Endocrinology Department of Centro Hospitalar de Lisboa Central, between January of 2008 and July of 2015. Demographic characteristics, underlying and ocular disease, referral and follow-up of these patients in the Pediatric Ophthalmology Department were evaluated.

Medical records of 304 patients with type 1 diabetes were analyzed. 110 patients referred to Ophthalmology Department had been included in the study. The mean age was 13.2 ±3.24 years (4-20 years), 57 were male and 53 female. Type 1 diabetes was diagnosed at 7.5 ±3.0 years on average (0.75-13 years) and mean disease duration was 6.0 ±3.3 years (1-14 years). The average of the last hemoglobin A1c value was 8.6% ±1.5 (4.9-14.4%). The first eye exam was performed at 9.4 ±3.1 years on average (2-19 years), in 55 cases the patients had less than 10 years and, of those, 29 were referred in the first year after diagnosis (mean duration diabetes of 2.0 ±0.7 years; 0-7 years). Regarding the 55 patients older than 9 years, 27 were referred in the first year after diagnosis (mean duration of diabetes 2.3 ±0.8 years, 0-9 years). In 54 patients ophthalmological exam was repeated after 1 year, 15 after 2 years, 1 after 3 years and 1 after 5 years. No diabetic retinopathy cases were found. 28 astigmatism, 12 hyperopia, 16 myopia, 5 strabismus, 2 blepharoptosis and 1 polar cataract were diagnosed.

International Society for Pediatric and Adolescent Diabetes recommend ophthalmological initial screening 2 years after the diagnosis of type 1 diabetes, in patients above 10 years, and 5 years after, if lower ages. American Academy of Ophthalmology 2014 guidelines recommend that the first eye examination should begin 5 years after the diagnosis and repeated annually. A previous study conducted at Hospital Dona Estefânia, between 1999 and 2000, by Rodrigues P et al has described a low incidence of ocular lesions (6.4%) in the studied population, being in agreement with our results. Recent published studies are also consistent and demonstrate that the rare incidence of ocular complications of diabetes until puberty can justify new guidelines in the coming years.

Key-words

Diabetes Tipo 1, Patologia Ocular, Idade Pediátrica, Rastreio, Retinopatia

INTRODUCTION

Type 1 diabetes is the most common metabolic disease in children.[1] In Portugal, 0,16% of people aged between 0 and 19 years-old are affected by type 1 diabetes. During 2013, 18,2 new cases were diagnosed per 100000 children aged 0 to 14 years-old.[2]

Duration of disease and metabolic control are the most important risk factors for the development of ocular complications. Genetic load has shown to constitute an important influence in this chapter.[3]

Although specialized care have also been contributing to the reduced number of ocular complications in pediatric age in developed countries, diabetic retinopathy (DR) is still the leading cause of blindness worldwide.[4] To the extent of current knowledge, these findings are rare until puberty age.[3,5] Nevertheless, the age at diagnosis and prevalence of DR in pediatric age are not well established and there is little of information about the onset and prevalence of other ocular complications because the majority of studies have focused on DR.

In order to prevent and treat the ocular manifestations of this disease, a correct monitorization should include adequate metabolic control achievement, search for related risk factors, effective screening implementation programs and treatment modalities optimization.

The effectiveness of existing guidelines for ocular screening in this group is unclear because of ocular pathology low prevalence in younger ages and the paucity of studies regarding this subject. The authors intend to review the prevalence of ocular disease in a group of children with type 1 diabetes, including DR, cataract, refractive error and strabismus.

MATERIAL AND METHODS

The authors performed a retrospective study of type 1 diabetes' patients registered and monitored in Pediatric Endocrinology Department of Centro Hospitalar de Lisboa Central since January of 2008 to July of 2015. Current study was based on electronic medical records consultation. Patients that were referred to the Ophthalmology Department for observation were included. Study protocol was approved by Centro Hospitalar de Lisboa Central Administrative Council.

Collected data included age, gender, race, child's age at diagnosis of diabetes, diabetes duration, mean hemoglobin A_{1c} (HbA_{1c}) in the past three years, most recent HbA_{1c}, comorbidities, age at first eye examination and last one, number of eye exams and their frequency, presence and description of retinopathy, refractive error, strabismus, blepharoptosis and cataract. Retinopathy screening was performed with dilated fundoscopic examinations by pediatric ophthalmologists. Refractive errors were obtained by cycloplegic refractions and classified by the amount of spherical equivalence (in diopters [D]). High myopia was considered if ≥4.0 D of myopia, high hyperopia if ≥3.0 D of hyperopia and high astigmatism was defined as ≥1.5 D cylindrical refractive error. High refractive error was defined as the presence of 1 or more of high myopia, high hyperopia and high astigmatism. Descriptive statistics (mean, minimum and maximum) were calculated for baseline characteristics of the subjects.

A literature analysis was performed based on a PubMed search for the keywords: type 1 diabetes, ocular disease, pediatric age, screening and retinopathy.

RESULTS

A total of 304 medical records of patients with type 1 diabetes were analyzed. 110 patients had been referred to Ophthalmology Department being included in the study.

Baseline characteristics of these subjects are shown in Table 1. The mean age was 13.2 ±3.24 years (4-20 years), 57 were male and 53 female. Race was not specified in the majority of cases. Type 1 diabetes was diagnosed at 7.5 ±3.0 years on average (0.75-13 years) and mean disease duration was 6.0 ±3.3 years (1-14 years). The average of HbA_{1c} in the three years was 9.2% ±1.8 (4.7-14.9%). The average of the last HbA1c value was 8.6% ±1.5 (4.9-14.4%).

Tabela 1 |

Age	
Mean	13.2
Minimum (min.)	4
Maximum (max.)	20
Standard Deviation (SD)	3.24
Gender - n (%)	
Male	57 (51.8%)
Female	53 (48.2%)
Age at diabetes diagnosis (years [yrs])	
Mean	7.5
Min.	0.75
Max.	13
SD	3.0
Diabetes duration (yrs)	
Mean	6.0
Min.	1
Max.	14
SD	3.3
HbA1c in the last 3 years (%)	
Mean	9.2
Min.	4.7
Max.	14.9
SD	1.8
Last HbA1c (%)	
Mean	8.6
Min.	4.9
Max.	14.4
SD	1.5

Data regarding eye examination is described in Table 2. The first eye examination was performed at 9.4 ±3.1 years on average (2-19 years), in 55 cases the patients had less than 10 years and, of those, 29 were referred in the first year after diagnosis (mean duration diabetes of 2.0 ±0.7 years; 0-7 years). Regarding the 55 patients older than 9 years, 27 were referred in the first year after diagnosis (mean duration of diabetes 2.3 ± 0.8 years, 0-9 years). In 54 patients ophthalmological exam was repeated after 1 year, 15 after 2 years, 1 after 3 years and 1 after 5 years. The remainder were not specified.

Tabela 2 |

Age at first eye examination (yrs)	
Mean	9.4
Min.	2
Max.	19
SD	3.1
< 10 years-old	**55**
In the 1st year of diagnosis	29
Diabetes duration (yrs)	
Mean	2.0
Min.	0
Max.	7
SD	0.7
≥ 10 years-old	**55**
In the 1st year of diagnosis	27
Diabetes duration (yrs)	
Mean	2.3
Min.	0
Max.	9
SD	0.8
Re-evaluation	
1 year	54
2 years	15
3 years	1
5 years	1

Ocular findings are described in Table 3. No children were found to have diabetic retinopathy during the period of the study. 1 case of congenital unilateral posterior polar cataract was found (0.9%), with normal visual acuity. 1 patient (0.9%) with Kearns-Sayre syndrome was found to have exotropia. 28 patients (25.5%) were found to have astigmatism, including 6 cases of high astigmatism (5.5%). 16 children (14.5%) had myopia, including 3 cases of high myopia (2.7%). 12 cases (10.9%) of hyperopia were registered, 1 of high hyperopia (0.9%). High refractive error was found in 10 patients (9.1%).

Tabela 3 |

Diabetic retinopathy - n (%)	0 (0%)
Cataract - n (%)	1 (0.9%)
Strabismus - n (%)	**5 (4.5%)**
Phoria	4 (3.6%)
Tropia	1 (0.9%)
Blepharoptosis - n (%)	2 (1.8%)
Refractive error - n (%)	**56 (50.9%)**
Myopia	16 (14.5%)
Mean age of diagnosis (yrs)	8.6 ±0.8
Hyperopia	12 (10.9%)
Mean age of diagnosis (yrs)	6.1 ±0.4
Astigmatism	28 (25.5%)
Mean age of diagnosis (yrs)	7.2 ±1.1
High refractive error	10 (9.1%)
Mean age of diagnosis (yrs)	9.1 ±1.3

DISCUSSION

A group of 110 type 1 diabetic patients (4-20 years; mean 13.2 ±3.24) was studied, providing important data about their referral to ocular screening and the prevalence of ocular findings in a tertiary center. The first eye exam was performed at 9.4 ±3.1 years on average (2-19 years) and in 50% of the initial exams children were less than 10 years-old. The majority of these earlier exams might be explained by ocular complaints or in the context of preschooler screening. Annual screening was the most commonly observed regimen. One limitation of our study was the chosen technique for screening. In all cases, dilated fundoscopic examinations were performed by pediatric ophthalmologists. The use of fundus photography has been found to be more sensitive than fundoscopy for detecting mild retinopathy, particularly in children, who are more difficult to examine than adults.[6]

In our study, we didn't find any case of DR. Geloneck M *et al*[7] in 2015, have reviewed the literature to identify 12 studies reporting the occurrence of DR during childhood (published between 1981 until 2012) and verified that reported prevalence of DR among children was 9% to 28%. Probable explanations for this wide range of prevalence are the differing baseline characteristics (ages at examination and metabolic control), different screening modalities and the improvements in the provided care to these patients over time. They have also found that the shortest duration of diabetes before the development of proliferative DR was 5 to 6 years and the earliest documented age of severe DR was 15 years-old.[7]

Regarding the incidence of cataract, in our study we found 1 case of posterior polar cataract (0.9%), with no commitment of visual function. Reported incidence of diabetic cataract is 0.7% to 3.4%.[8,9] Posterior subcapsular, lamellar, flakelike and dense milky-white cataracts are the described morphologies.8,9 To the best of our knowledge, none association was reported between posterior polar cataract and diabetes.

The prevalence of high refractive errors and strabismus in our study was found to be similar to a nondiabetic pediatric population.[10,11,12]

A previous study conducted at Hospital Dona Estefânia, between 1999 and 2000, by Rodrigues P *et al* described a low incidence of ocular lesions (6.4%) in studied population, being in agreement with our results. They described 1 case of a 17-year-old girl with non-proliferative DR (1.6%), 11 years after the diagnosis of diabetes, and 3 cases of bilateral cataract (4.8%).[13]

International Society for Pediatric and Adolescent Diabetes recommend initial screening 2 years after the diagnosis of type 1 diabetes, in patients above 10 years, and 5 years after, if lower ages.[14] American Academy of Pediatrics guidelines suggest initiating annual examinations 3 to 5 years after diabetes diagnosis or after the age of 9 years, whichever occurs later.1 American Academy of Ophthalmology 2014 guidelines recommend that the first eye examination should be performed 5 years after the diagnosis and repeated annually.[4] The heterogeneity of current guidelines related to the age of first ophthalmological examination in diabetic children demonstrate that the prevalence of ocular complications must be noticed, in order to allow the improvement and concordance of recommended strategies.

Results obtained in our retrospective review are in agreement with published studies. The development of diabetic retinopathy until puberty is rare. The occurrence of refractive errors and strabismus are similar to healthy children.

In conclusion, the rare incidence of ocular complications of diabetes until puberty can justify new guidelines in the coming years. An effort to enhance the screening of ocular disease according to the age and the most frequent related diseases should be performed.

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