



Trabajo Original

Diagnosis of night blindness through standardized interview and electroretinography *Diagnóstico de la ceguera nocturna mediante entrevista normalizada y electroretinografía*

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Abstract

Introduction: vitamin A deficiency (VAD) is one of the biggest problems in public health worldwide, and night blindness (NB) is the first functional change caused by deficiency of this vitamin. In this context, electroretinography stands out as the gold-standard diagnostic method; however, it is a high-cost method and its applicability in clinical practice presents some difficulties.

Objective: to compare NB diagnosis through the use of the standardized interview issued by the World Health Organization/Pan American Health Organization (WHO/PAHO) and with electroretinography, and to evaluate the association of these diagnoses with serum concentrations of retinol in individuals with class III obesity.

Methods: adult patients of both genders, in the 20-60 years age group, with BMI ≥ 40 kg/m², were studied. NB was diagnosed through electroretinography and the standardized interview validated by the WHO/PAHO. Serum retinol was quantified by the HPLC-UV method, and VAD was diagnosed when levels were < 1.05 $\mu\text{mol/L}$; severity was also evaluated. The statistical analysis was carried out using the Statistical Package for the Social Sciences, version 21.0 ($p < 0.05$).

Results: mean BMI was 44.9 ± 11.8 kg/m², and a negative correlation was found for serum levels of retinol ($p = 0.01$). The prevalence of VAD, according to the serum concentration of retinol, was 14 %; of this percentage 23.3 % had NB according to the standardized interview, and 22.0 % according to electroretinography. NB as diagnosed by both methods showed an association with VAD according to serum concentrations of retinol. Of these individuals with NB, according to the standardized interview, 6.9 % had severe VAD, 10.3 % moderate VAD, and 82.8 % marginal VAD.

Conclusion: the standardized interview for the diagnosis of NB can be a good strategy to evaluate the nutritional status of vitamin A, and it is a simple, non-invasive, low-cost method.

Keywords:

Night blindness.
Serum retinol.
Electroretinography.
Class III obesity.
Vitamin A deficiency.

Resumen

Introducción: la deficiencia de vitamina A (DVA) es uno de los mayores problemas de salud pública a escala mundial, y la ceguera nocturna (CN) es el primer cambio funcional causado por la falta de esta vitamina. En este contexto, la electroretinografía se destaca como el método de diagnóstico de referencia; sin embargo, es un método de coste elevado y su aplicabilidad en la práctica clínica presenta algunas dificultades.

Objetivo: comparar el diagnóstico de CN mediante el uso de la entrevista estandarizada de la Organización Mundial de la Salud/Organización Panamericana de la Salud (OMS/OPS) con la electroretinografía, y también evaluar la asociación de estos diagnósticos con las concentraciones séricas de retinol en las personas con obesidad de clase III.

Métodos: se estudiaron pacientes adultos de ambos sexos, en el grupo de 20 a 60 años de edad y con IMC ≥ 40 kg/m². La NB se diagnosticó mediante electroretinografía y la entrevista estandarizada validada por la OMS/OPS. El nivel sérico de retinol se cuantificó mediante el método HPLC-UV, y el DVA se diagnosticó cuando los niveles eran < 1.05 $\mu\text{mol/L}$; también se evaluó la gravedad. El análisis estadístico se realizó a través del Paquete Estadístico para las Ciencias Sociales, versión 21.0 ($p < 0,05$).

Resultados: el IMC promedio fue de $44,9 \pm 11,8$ kg/m² y se encontró una correlación negativa en los niveles séricos de retinol ($p = 0,01$). La prevalencia de DVA, según las concentraciones séricas de retinol, fue del 14 %; de este porcentaje, el 23,3 % tenían NB de acuerdo con la entrevista estandarizada y el 22,0 % según la electroretinografía. La NB diagnosticada por ambos métodos mostró asociación con el DVA según las concentraciones séricas de retinol. De estos individuos con NB, según la entrevista estandarizada, el 6,9 % tenían VAD grave, el 10,3 % VAD moderado y el 82,8 % VAD marginal.

Conclusión: la entrevista estandarizada para el diagnóstico de NB puede ser una buena estrategia para evaluar el estado nutricional de la vitamina A y es un método simple, no invasivo y de bajo coste.

Palabras clave:

Ceguera nocturna.
Retinol sérico.
Electroretinografía.
Obesidad de clase III.
Deficiencia de vitamina A.

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INTRODUCTION

Vitamin A deficiency (VAD) is one of the most prevalent health problems worldwide (1). According to the World Health Organization (2), 45 countries have this problem at a clinical level, and 122 have a subclinical shortage of this vitamin, in which individuals have marginal liver stores. Despite the progress made in the evaluation of the clinical signs of deficiency, marginal VAD is still prevalent and difficult to diagnose (3,4).

Vitamin A has been highlighted by its performance against free radicals, protecting the body against oxidative stress and, consequently, preventing damage and tissue lesions related to various non-communicable chronic diseases, the primary cause of morbidity/mortality at present (5,6,7).

In addition, vitamin A participates in functions related to the ocular system and plays a fundamental role in the maintenance of integrity in visual processes such as the need to visually adjust to low-light environments (8,9). VAD can progress to more advanced stages in which functional alterations have already resulted in ocular changes (10). Night blindness (NB) is the first of these alterations, characterized by a decrease in night vision acuity and normal vision during the day (11,12).

The standardized questionnaire designed by the World Health Organization (WHO) and the Pan-American Health Organization (PAHO) is used as a functional indicator of VAD in the diagnosis of NB, especially in at-risk population segments such as pregnant women and preschoolers (13). In this regard, Sommer and co-workers (1980) proved the validity of this questionnaire for preschoolers, while Saunders and co-workers (2004/2005) adapted and validated it for pregnant women (11,14,15).

It is noted that Pereira and co-workers (2011) also validated the WHO/PAHO standardized interview for the diagnosis of NB in individuals with obesity, showing its association with the serum concentrations and liver stores of retinol. Such conduct is regarded as important when we consider the inverse relationship between VAD and body mass index (BMI) (16,17,18).

However, there is still no study in the literature that compares the diagnosis of NB, obtained from the standardized interview, with the use of electroretinography in population segments with potential risk for development of this vitamin deficiency. Thus, this study aims to compare the diagnosis of NB through both the use of the WHO/PAHO standardized interview and electroretinography, besides the association of these diagnoses with the serum concentrations of retinol in adult individuals with obesity.

METHODS

A cross-sectional study was carried out in adults with class III obesity followed up by the Multidisciplinary Center for Bariatric and Metabolic Surgery in the municipality of Rio de Janeiro. Inclusion criteria for the study were: a) patients of both genders; b) aged 20-59 years; c) body mass index (BMI) ≥ 40 kg/m²; d) absence of use of vitamin supplements and lipid drugs; e) absence of prior bariatric surgery or gastrointestinal tract surgery;

f) not during pregnancy or lactation; g) absence of liver diseases, except non-alcoholic fatty liver disease.

In the evaluation of the nutritional status of vitamin A, biochemical (serum concentrations of retinol) and functional (WHO/PAHO standardized interview and electroretinography) indicators were included.

For the evaluation of the serum concentrations of retinol, an aliquot of 5 mL of blood was collected after an overnight fast of at least 8 hours, and high-efficiency liquid chromatography (HPLC-UV) was the quantification method used (WHO, 1996). In the present study, serum retinol levels > 1.05 $\mu\text{mol/L}$ were considered adequate, and a cut-off point < 1.05 $\mu\text{mol/L}$ was used to indicate VAD (19,20,21).

For the evaluation of VAD severity, the serum values of retinol obtained were compared to the normality cut-off points proposed by the World Health Organization (WHO, 1996) in interval classes of 0.35 $\mu\text{mol/L}$. Thus, VAD was classified as severe (< 0.35 $\mu\text{mol/L}$), moderate (≥ 0.35 $\mu\text{mol/L}$, < 0.70 $\mu\text{mol/L}$) and mild (≥ 0.70 $\mu\text{mol/L}$, < 1.05 $\mu\text{mol/L}$) (22).

The WHO (1996) and PAHO (McIaren & Frigg, 1999) standardized interview diagnosed NB when the respondent reported difficulty in seeing in dim light or at night, and no difficulty in seeing during the day (22,10).

The interview was performed using simple language and examples cited included difficulty in recognizing people and identifying objects in low-lighting places, difficulty in walking in the dark or in low-lighting places, and the ability to adjust vision when entering tunnels, projection rooms, etc., that is, common day-to-day situations for the respondents (8,11).

Electroretinography (ERG) was performed according to the protocol of the International Society for Clinical Electrophysiology of Vision (ISCEV) (23) to evaluate retinal cells (cones and rods). Cones are responsible for sharpness of vision, detail, and color vision. Rods are responsible for peripheral vision and night vision.

The examination was carried out through a contact lens placed on both eyes and an electrode placed at the temple or periorbital region. Then, luminous stimuli were provided with various intensities in the color white, red and blue, and after adaptation to darkness and light they were collected on a screen and analyzed. It is an examination considered to be painless, without complications, and is acknowledged as the gold standard for evaluation of these cells and for diagnosis of NB.

After the luminous stimuli, responses were evaluated according to the ISCEV, namely: a) scotopic response to rods; b) maximum scotopic response (cones and rods); c) scotopic response to oscillatory potentials; d) photopic response to single-flash cone; and e) photopic response to 30-Hertz flicker.

NB was diagnosed when electroretinography showed a reduction in the amplitude of the scotopic response (adaptation to darkness), with a normal photopic response (adaptation to light).

Aiming to standardize the procedures, the standardized interview for NB research was applied by a single interviewer. The reliability assessment of the diagnosis of NB based on the interview was carried out through a 10 % retest of the sample conducted upon the patient's return to the next visit.

After the evaluation of nutritional status and vitamin A, patients with VAD according to the functional indicator, electroretinography, and/or biochemical indicators, were treated with vitamin A supplementation (5,000 IU/day) and received nutritional guidance.

The statistical analysis included central tendency measures, Student's t-test, Spearman's correlation, and the Chi-square test. The significance level established was 5 %. Analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 21.0.

This study was approved by the Research Ethics Committee of the University Hospital Clementino Fraga Filho (Research Protocol No. 011/10 – CEP).

The validity of the interview for the diagnosis of NB was evaluated using electroretinography and biochemical indicators (serum levels of retinol), and sensitivity, specificity and accuracy were calculated (24).

RESULTS

The sample comprised 30 patients with class III obesity, mostly women (75.5 %). The sample mean age was 35.0 ± 11.6 years and mean BMI was 44.9 ± 11.8 kg/m², whereas serum levels of retinol were $1.21 \mu\text{mol/L} \pm 0.58 \mu\text{mol/L}$. According to this indicator, 14 % of the sample had VAD ($< 1.05 \mu\text{mol/L}$). Dividing the sample into interval classes, 62.5 % had marginal VAD, 25 % moderate VAD and 12.5 % severe VAD.

According to electroretinography, 22.0 % of the individuals presented NB. According to the standardized interview, 23.3 % of the individuals presented NB. Considering VAD interval classes, 6.9 % of the individuals diagnosed with NB, according to the standardized interview, had severe VAD, 10.3 % moderate VAD and 82.8 % marginal VAD.

Among the individuals with NB, both methods presented a significant association between NB occurrence and inadequacy of serum concentrations of retinol. According to electroretinography, 80.0 % of the individuals diagnosed with NB presented serum inadequacy of retinol ($p = 0.015$); according to the standardized interview, 71.4 % ($p < 0.01$) serum inadequacy of retinol (Table I). There was no significant difference in the diagnosis of NB between both methods ($p > 0.05$).

For the standardized interview, validation, sensitivity, specificity and accuracy were evaluated in relation to serum levels of retinol. The sensitivity found was 71.4 %, that is, this was the capacity of the interview to determine the percentage of NB cases. Regarding specificity, the method identified 91.3 % of individuals with absence of NB. Regarding accuracy, it may be said that the interview correctly classified 86.7 % of the NB cases diagnosed according to serum retinol levels.

The same analyses carried out with the gold standard electroretinography, in comparison with the serum levels of retinol, found 85.7 % for sensitivity and 95.7 % for specificity. Regarding accuracy, electroretinography correctly classified almost 93.3 % of the NB cases.

Table I. Association between presence of night blindness, according to the WHO/PAHO standardized interview and electroretinography, and adequacy of serum retinol levels in class III obesity individuals

	Serum retinol		p-value
	Inadequate (< 1.05 $\mu\text{mol/L}$)	Adequate (> 1.05 $\mu\text{mol/L}$)	
	n (%)	n (%)	
Standardized interview			
Presence of NB	5 (71.4)	2 (28.6)	< 0.01
Absence of NB	2 (8.7)	21 (91.3)	
Electroretinography			
Presence of NB	6 (80.0)	1 (20.0)	0.015
Absence of NB	1 (20.0)	22 (80.0)	

Chi-Square test ($p < 0.05$). NB: night blindness.

DISCUSSION

Vitamin A deficiency has been considered a public health problem, and it has been especially investigated in the classic risk groups, such as pregnant women, mothers and preschool-age children. However, due to the participation of vitamin A in different metabolic processes, and mainly by its association with body adiposity and chronic inflammation, which increases the demand of this nutrient, the need for monitoring nutritional Vitamin A status in other population groups has already been shown (18,25).

Obesity has been recognized as a risk factor for several metabolic and nutritional alterations such as VAD. In the present study, a significant negative association was found between BMI and serum concentrations of retinol. This association has been described in the literature highlighting the role of vitamin A in body adiposity (26,27,28,29).

In this sense, the study of Pereira and co-workers (2012) is worth highlighting on account of its great contribution to the evaluation of the nutritional status of vitamin A when it validated the PAHO/WHO standardized interview for the diagnosis of NB in individuals with obesity, showing its association with the serum concentrations and liver stores of retinol (18).

According to the World Health Organization (2014), NB is the first functional manifestation of VAD, and its prevalence occurs with increased severity of this vitamin deficiency (serum concentrations $< 0.7 \mu\text{mol/L}$) (30). However, in our study we observed that among the individuals who had VAD, 82.8 % had serum values of retinol between ≥ 0.70 and $< 1.05 \mu\text{mol/L}$ (mild VAD), and an association was found between the serum inadequacy of retinol and the presence of NB. Similar results were found in studies with pregnant women where NB may have affected percentages ranging from 38.5 % to 82.8 % of the women classified

with mild VAD (serum concentrations of retinol ≥ 0.70 and < 1.05 $\mu\text{mol/L}$) (4,11).

From these results, it is observed that NB can develop with serum levels of retinol < 1.05 $\mu\text{mol/L}$, thus confirming that this functional alteration may occur in the presence of physiologically acceptable circulating levels of retinol (WHO, 2014). Given this, early diagnosis from an easy-to-apply indicator becomes essential in routine health-care protocols.

The use of simple methods, such as the standardized interview, only addressed to VAD at-risk segments, limits early interventions, which could prevent the high prevalence of this deficiency in individuals with diseases with a large social impact. In the present study, approximately one-third of the individuals with class III obesity presented NB according to the standardized interview, emphasizing the importance of applying this method to the aforementioned population.

Regarding public health, tests with good sensitivity and specificity characterized by an easy and low-cost application are highlighted due to their relevance. In the present study, a high sensitivity and specificity was found not only for the standardized interview (71.4 % and 91.3 %, respectively) but also for the gold standard (85.7 % and 95.7 %, respectively). In addition, both techniques were associated with inadequacy of serum retinol, with no significant difference between them.

Thus, the use of the standardized interview for the diagnosis of NB can be compared to the gold standard, electroretinography, thus enabling the evaluation of this functional alteration at different levels of health care, optimizing the diagnosis and the earliest use of a therapeutic treatment for NB.

These findings are of great clinical relevance, if we consider the high cost involved in the conduction of electroretinography, which requires qualified professionals, besides the difficulty of its implementation in routine clinical practice. Furthermore, the diagnosis obtained through the standardized interview shows a simple, validated method that is able to detect alterations in the visual function, still in the VAD mild phase, according to the classification of the serum concentrations of retinol.

As far as we know, this study is the first in the literature that seeks to compare the diagnosis of NB as obtained from the standardized interview with the use of electroretinography, a test considered to be the gold standard for the diagnosis of NB, in a population segment other than those traditionally regarded as the segments at risk for vitamin A deficiency.

CONCLUSION

The standardized interview for the diagnosis of NB has shown to be a promising strategy to assess the nutritional status of vitamin A, and it is a simple, non-invasive, low-cost diagnostic method.

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