INTER-OBSERVER VARIABILITY IN THE DIAGNOSIS AND CLASSIFICATION OF DIABETIC RETINOPATHY THROUGH BIOMICROSCOPY

VARIABILIDAD INTEROBSERVADOR EN EL DIAGNÓSTICO Y CLASIFICACIÓN DE LA RETINOPATÍA DIABÉTICA MEDIANTE BIOMICROSCOPÍA

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ABSTRACT

Objective: Analysis of the inter-observer variability of biomicroscopy used for the diagnosis of Diabetic Retinopathy.

Methods: This was a descriptive study. Parallel observer-blind evaluations of the degree of retinopathy in type 2 diabetic patients, as defined on biomicroscopic photographs, were performed by two ophthalmologists. The sample size required for the Kappa index among ophthalmologists with a disagreement ratio of 15%, precision ratio of 5% and confidence level of 95% is n=196 («n» being the number of eyes). The only variable measured was the degree of Diabetic Retinopathy, according to the modified Early Treatment Diabetic Research Study (ETDRS) classification.

Results: The average age of the 217 patients photographed was 65.42 years (SD= 9.91). In 191 instances there was total agreement between the 2 ophthalmologists. In 24 instances the discrepancy was only of one degree of the classification of the ETDRS.

RESUMEN

Objetivo: Análisis de la variabilidad interobservador de la biomicroscopía utilizada para el diagnóstico de retinopatía diabética.

Métodos: Diseño: Observacional descriptivo. Valoración en paralelo, de forma ciega para los observadores, del grado de retinopatía diabética mediante biomicroscopía en pacientes diabéticos tipo 2. Muestra: Para la evaluación del índice Kappa, con una estimación de una proporción de desacuerdo del 15%, (precisión del 5% intervalo de confianza del 95%) muestra n=196, (siendo «n» el número de ojos). Variables a medir: grado de retinopatía diabética, según la clasificación del ETDRS modificada.

Resultados: La edad media de los pacientes fotografiados fue de 65,42 años (DE= 9,91). De las 217 biomicroscopías realizadas, en 191 se encontró concordancia total. En 24 la discordancia fue tan sólo en un grado de la clasificación del ETDRS, en 2 la discordancia fue en dos grados. En ningún caso fue mayor. Kappa ponderado cuadrático = 0,876,
INTRODUCTION

Diabetes Mellitus type 2 (DM2) is a health problem which is gaining relevance. In Spain, its prevalence in the population over 30 ranges between 6.4 and 10.3%, with 3.5-5.9% being undiagnosed (1-3).

Diabetic Retinopathy (DR) is one of the most important complications of DM2. Highly variable prevalence rates of DR have been described, ranging from 15 to 50% and even higher, depending on evolution time (4,5).

The diabetic population exhibits a relative loss of vision risk twenty times above that of the non-diabetic population (6). DR is the cause of 70-80% of diabetes-induced blindness and has become the main cause of visual deficit and blindness in adults between 20 and 74, appearing in approximately 5% of patients with DM2 ten years after being diagnosed (7).

DR screening is of great importance because when loss of visual acuity emerges it is usually late for an efficient treatment. The treatment of choice would be laser photocoagulation in order to avoid or delay vision loss in a high number of patients with non-proliferative severe DR and proliferative DR (8).

Accordingly, the most extended general recommendation is an annual exploration of all diabetic patients, but this period can be extended in the absence of risk factors or lesions (9). This could impose a burden of work on units specialized in ocular diabetes, which would imply the existence of patients with severe forms in waiting lists. The most efficient form of screening DR is to obtain images of the retina for classification. There are multiple studies which attempt to validate this technique comparing it with the biomicroscopy carried out by ophthalmologists (10-17) or by opticians (18).

However, there are no studies which have assessed the inter-observer variability of biomicroscopy even though the explorations carried out by a single ophthalmologist are utilized as a standard reference pattern. The present study endeavors to address this uncertainty.

SUBJECTS, MATERIAL AND METHODS

Design

Observational descriptive. Parallel assessment, blind for observers of the degree of diabetic retinopathy by means of biomicroscopy.

Subjects of the study

Diabetic patients type 2. The type one diabetic patients and those who received laser photocoagulation treatment were excluded.

Study sample, sampling and framework

The main task was to assess the Kappa index (19). Considering the problem as the estimate of a proportion of disagreement and assuming that this
is in the range of 15%, a precision of 5% could be obtained for a confidence interval of 95% with a Sample of size n=196 («n» being the number of eyes and not of diabetic patients) (20).

The sample comprised 217 eyes of patients with DM 2 selected in a consecutive manner when attending the practice in the health centre and being referred to the ophthalmology service of our hospital, both in the capital city of Huelva.

Variables to be measured

Degree of diabetic retinopathy according to the modified ETDRS classification (21).

Informed Consent

The study protocol was approved by the research committee. The individuals selected for the study were informed verbally and in writing about its content, requesting them to sign their consent.

Data collection and techniques for measuring variables

Two ophthalmologists carried out the blind biomicroscopy studies on the patients in the same day. The variables for the study and the patient data were collected by each ophthalmologist independently in a specially prepared sheet.

The exploration was carried out with slit lamp and a 66- dioptre non-contact lens (VOLK Super 66®). A contact lens was utilized (Ocular MAINSTER Standard Focal/Grid)® if vision was not adequate.

Data were also collected on transparency: cataract (≤ grado 2), corneal leucoma and vitreous opacities.

Data analysis: the linear pondered and quadratic kappa index was utilized to assess the match between the biomicroscopy reading of the ophthalmologists because it allowed to allocate different weights according to the degree of mismatch (22,23).

The scale proposed by Landis and Koch (24) was utilized for assessing the matching degree of the Kappa index (table I).

The statistical analysis programs utilized in this study were: Access® database for data collection, SPSS® statistical program (SPSS for Windows, SPSS Inc, Chicago, USA) and Excel® spreadsheet (Excel for Windows, Illinois, USA) for calculating the Kappa index.

RESULTS

The mean age of photographed patients was 65.42 years (SD= 9.91), with the youngest being 35 and the eldest 89 (fig. 1).

In five eyes it was not possible to carry out the exploration (both ophthalmologists considered said eyes unfit for exploration), one due to enucleation, two due to highly evolved cataracts, one due to chronic retinal detachment and one for unspecified reasons.

Of 217 eyes subjected to biomicroscopy, a full match was found between both ophthalmologists for 191 eyes, with 151 being labeled as non-DR, 16 slight DR (SDR), 22 moderate DR (MDR) and 2 severe DR (SDR). In 24 the mismatch was only one

<table>
<thead>
<tr>
<th>K Value</th>
<th>Degree of matching</th>
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<tbody>
<tr>
<td>&lt; 0.20</td>
<td>Poor</td>
</tr>
<tr>
<td>0.21-0.40</td>
<td>Weak</td>
</tr>
<tr>
<td>0.41-0.60</td>
<td>Moderate</td>
</tr>
<tr>
<td>0.61-0.80</td>
<td>Good</td>
</tr>
<tr>
<td>0.81-1</td>
<td>Very good</td>
</tr>
</tbody>
</table>

Fig. 1: Age in years of photographed patients.
degree of the ETDRS classification, in 17 it was between NO DR and SDR, in five between SDR and MDR, one between MDR and SDR and one between SDR very severe diabetic retinopathy (VSDR). In two, the mismatch was of two degrees of said classification, between NO DR and MDR. In no case the mismatch exceeded two levels (Table II).

With the above results and the allocation of weight as established in table 3, we calculated the global matching between ophthalmologists, linear weighted Kappa = 0.804. CI 95%: 0.729-0.878.

With the above results and the allocation of weight as established in table 4, we calculated the global matching between ophthalmologists, squared weighted Kappa = 0.876. CI 95%: 0.655-0.952.

In nine out of 26 non-matching eyes medium transparency problems were found (34.62%), against 42 in 191 matching eyes (21.99%). Statistically non-significant difference P=0.1542.

DISCUSSION

The weighted Kappa was calculated with allocation of linear and Squared weights. There is a controversy in the literature about which is the most adequate. When assigning square weights, the value of Kappa tends to increase in proportion to the number of categories (25). In the case of DR, we considered the letter to have a greater value because it allocates a greater difference in weights the further away are the categories in the mismatches, which fits in better with the clinical transcendence of the test. It is different to be mistaken in one degree of retinopathy, for example between no retinopathy and slight retinopathy, than to confuse absence of retinopathy with severe retinopathy. In the first case, the error would be resolved without problems for the patient in the second visit, whereas in the second case it could be irreversible. Both were analyzed in order to compare them with the literature. In our case, the squared weighted Kappa index was of 0.876 which, according to the table proposed by Landis and Koch, represents a “very good” rate of matches (24). In any case, even if the linear weight allocation method was utilized, the result would be similar.

In addition to being small, the discrepancies have no clinical relevance because 92.3% represented only one degree in the ETDRS classification, and in the two cases (7.7%) of two degrees, the difference (between no retinopathy and moderate retinopathy) did not affect the treatment decision. The discrepancies never exceeded two degrees.

Even though no proliferative DRs were found, we do not consider this to be an inconvenient for validating the technique because of the objective is to screen lesions in type 2 diabetic patients from the community non-hospital environment, where the number of severe undiagnosed and untreated lesions is very low (26).

It is noteworthy that the medium transparency problems are 12% more frequent in non-matching eyes (non significant difference probably due to the

<table>
<thead>
<tr>
<th>Table II. Biomicroscopy matching between two ophthalmologists for diabetic retinopathy grades</th>
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<tbody>
<tr>
<td>NO DR</td>
</tr>
<tr>
<td>NO DR</td>
</tr>
<tr>
<td>LDR</td>
</tr>
<tr>
<td>MDR</td>
</tr>
<tr>
<td>SDR</td>
</tr>
<tr>
<td>VSDR</td>
</tr>
</tbody>
</table>

No diabetic retinopathy (NO DR); slight diabetic retinopathy (LDR); moderate diabetic retinopathy (MDR); Severe diabetic retinopathy (SDR); very severe diabetic retinopathy (VSDR).

<table>
<thead>
<tr>
<th>Table III. Weight allocation for calculating linear weighted Kappa</th>
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<tbody>
<tr>
<td>No DR</td>
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<tr>
<td>NO DR</td>
</tr>
<tr>
<td>LDR</td>
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<tr>
<td>MDR</td>
</tr>
<tr>
<td>SDR</td>
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<td>VSDR</td>
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</table>

No diabetic retinopathy (NO DR); slight diabetic retinopathy (LDR); moderate diabetic retinopathy (MDR); Severe diabetic retinopathy (SDR); very severe diabetic retinopathy (VSDR).

<table>
<thead>
<tr>
<th>Table IV. Weight allocation for calculating squared weighted Kappa</th>
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<tbody>
<tr>
<td>NO DR</td>
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<tr>
<td>NO DR</td>
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<tr>
<td>LDR</td>
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<tr>
<td>MDR</td>
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<tr>
<td>SDR</td>
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<td>VSDR</td>
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No diabetic retinopathy (NO DR); slight diabetic retinopathy (LDR); moderate diabetic retinopathy (MDR); Severe diabetic retinopathy (SDR); very severe diabetic retinopathy (VSDR).
small size of the sample), which gives rise to the possibility that after treating these problems the match would be even better.

The biomicroscopy taken by a single ophthalmologist is a reliable instrument as reference for diagnosing diabetic retinopathy.

REFERENCES