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#### Original article

# Interleukin-6 concentrations in the vitreous body of patients with retinal detachment\*



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#### ABSTRACT

Objective: To measure interleukin-6 (IL-6) levels in the vitreous body of patients with retinal detachment (RD).

Patients and methods: Undiluted vitreous samples were obtained from 40 patients with no history of prior vitreous or intraocular surgery. Patients were divided into two groups: A (n=20) patients with RD and B (n=20) patients with pre-retinal macular membranes and macular holes. IL-6 was determined using radioimmunoassay.

Results: IL-6 vitreous concentration in group A was  $122.4 \pm 16$  pg/mL (range 91.5–620) and in group B was  $46 \pm 23$  pg/mL (range 3–150) (p < .001).

Conclusions: These results show that the concentration of IL-6 in the vitreous body was significantly higher in patients with RD than in the control group.

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### Concentración de interleuquina-6 en el vítreo de pacientes con desprendimiento de retina

RESUMEN

Palabras clave: Interleuquina-6 Desprendimiento de retina Vítreo Membrana premacular Agujero macular Objetivo: Determinar los niveles de interleuquina-6 (IL-6) en el vítreo de pacientes con desprendimiento de retina (DdR).

Material y método: Mediante vitrectomía vía pars plana, se recogieron muestras no diluidas de vítreo de 40 pacientes sin antecedentes de cirugía vítrea o intraocular previa, que fueron divididos en 2 grupos: A (n=20) pacientes con DdR y B (n=20) pacientes con membrana premacular y agujero macular. La concentración de IL-6 se determinó mediante radioinmunoensayo.

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Resultados: La concentración vítrea de IL-6 en el grupo A fue 122,4  $\pm$  16 pg/mL (rango 91,5–620) y en el grupo B fue  $46\pm23$  pg/mL (rango 3–150) (p < 0,001).

Conclusiones: Estos resultados demuestran que la concentración vítrea de IL-6 está más elevada en los pacientes con DdR en comparación con el grupo control.

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#### Introduction

The retina is a complex neuronal tissue in which the first sensory transduction of visual stimuli takes place. It is formed by neuronal and non-neuronal cells organized in perfectly ordered layers. Retina detachment (RD) is the separation of the neurosensory retina and the pigment epithelium (RPE). When a detachment takes place the homeostasis of the retina is lost, involving morphological, biochemical and functional changes such as photoreceptor death, astrocyte proliferation and Müller cells, as well as new connections between neurons.<sup>1–4</sup> It is noteworthy that a significant number of photoreceptors can survive days and even weeks after RD. 1-4 This clinical observation, which has been reproduced in animal models, calls for considering a protection pathway (antiapoptosis) which maintains the feasibility of photoreceptors for a period of time.<sup>5-7</sup> Gene-microarray techniques were utilized to verify that 3 genes corresponding to interleukin 6 (IL-6) were activated in the antiapoptosis pathway.<sup>7–9</sup> The objective of the present paper is to determine the vitreous levels of IL-6 in patients with RD in comparison with patients without RD.

#### Subjects, material and methods

Overall, 40 eyes of 40 patients were included in the study. These were classified in 2 groups:

Group A with RD (n=20) and group B with premacular membrane and/or macular hole (n=20) (Tables 1 and 2). Inclusion criteria for group A patients were:

- The agreement to participate in the study, signing an informed consent;
- not having a diagnostic of diabetes mellitus;

#### Table 1 – Characteristics of Group A (n = 20).

Age, years (SD) 64.8 SD 11.4 Sex (M/F) 12/8

SD: standard deviation;F: female; M: male

#### Table 2 – Characteristics of Group B (n = 20).

Age, years (SD) 68.7 SD 11.7 Sex (M/F) 8/12 MH 5

MH: macular hole;SD: standard deviation; F: female; pRM: pre-retinal membrane; M: Male

- having a diagnostic of rhegmatogenous RD;
- authorization to access their clinical records.

The inclusion criteria for group B patients were:

- The agreement to participate in the study, signing an informed consent;
- not having a diagnostic of diabetes mellitus;
- not having a diagnostic of RD;
- authorization to access their clinical records.

The exclusion criteria comprised patients with previous vitrectomy, glaucoma and other vascular processes. In addition, samples with bleeding were also discarded. After performing 3 sclerotomies and placing the infusion cannula, the vitreotome was inserted in the central vitreous body, obtaining an undiluted sample of 0.3-0.5 mL in a syringe, subsequently opening the infusion and performing a 23 or 25 G vitrectomy. The samples were sent to the biochemistry lab, where they were frozen at  $-80\,^{\circ}$ C awaiting analysis. IL-6 levels were determined with radioimmunoassay. Statistical study: individual data were studied according to the Kruskal-Wallis global analysis, and when the values were statistically significant (p < 0.05) an individual comparative study was carried out with the nonparametric Mann–Whitney test. All the data were statistically processed with the SPSS 10.0 application (SPSS for Windows, SPSS Inc, Chicago, USA).

#### **Results**

In the present study, all the collected vitreous samples were undiluted as any dilution could affect the interpretation of results. In group B, the IL-6 values were low, with a mean value in the vitreous of  $46\pm23\,\mathrm{pg/mL}$  (range between 3 and 150 pg/mL). In group A, in all the samples levels were well those observed in group B, with a mean value in the vitreous of  $122.4\pm16\,\mathrm{pg/mL}$  (range between 91.5 and 620 pg/mL) (p=0.0008, nonparametric Mann–Whitney). In addition, a significant correlation was observed between IL-6 and the time elapsed since detachment ( $r^2=0.44$ , p=0.0116).

#### Discussion

Retina detachment is defined as the separation of the neurosensory retina from the underlying pigment epithelium, causing the death of photoreceptors due to apoptosis. Apoptotic pathway activation begins almost immediately after pigment epithelium separation, peaking on day 3.1 When photoreceptors, which are cells having a very high metabolic

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