Original article

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

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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 ± 16 pg/mL (range 91.5–620) and in group B was 46 ± 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.

Concentración de interleuquina-6 en el vitreo de pacientes con desprendimiento de retina

Resumen

Objetivo: Determinar los niveles de interleuquina-6 (IL-6) en el vitreo de pacientes con desprendimiento de retina (DdR).

Material y método: Mediante vitrectomía vía pars plana, se recogieron muestras no diluidas de vitre de 40 pacientes sin antecedentes de cirugía vitrea 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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Results: La concentración vitrea de IL-6 en el grupo A fue 122.4 ± 16 pg/mL (rango 91.5–620) y en el grupo B fue 46 ± 23 pg/mL (rango 3–150) (p < 0.001). 

Conclusions: Estos resultados demuestran que la concentración vitrea 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.1–4 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.3–5 Gene-microarray techniques were utilized to verify that 3 genes corresponding to interleukin 6 (IL-6) were activated in the antiapoptosis pathway.6–9 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;
- 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 vitrectome 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 25G vitrectomy. The samples were sent to the biochemistry lab, where they were frozen at ~80 °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 ± 23 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 ± 16 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
demand, are separated from their nutritional support, immediate death could be expected. Even though the thickness of the external nuclear layer diminishes between the first and third day after detachment, a significant number of photoreceptors survive even weeks later. Only if the retina is detached for a prolonged period of time, the majority of photoreceptors die. Clinical experience in retina detachment surgery has demonstrated the existence of a therapeutic window during which it is possible to repair the damage, preserving adequate visual acuity. Several series have demonstrated that a significant number of patients with macula-off maintain relatively good visual acuity with surgery between 5 and 10 days post-detachment. This suggests that neuroprotective factors (antiapoptosis) become activated at the retinal level to counterbalance the apoptosis activation produced by the retina-RPE separation.

Utilizing micro-array techniques it was possible to detect increased gene expression related to IL-6. The latter is a multifunction cytokine which is active in inflammation, hematopoiesis, angiogenesis, cell differentiation and neuronal protection. In neurons, IL-6 increases cellular survival. In retinal ischemia/perfusion models, the life of cells increases, increasing the transcription of IL-6 or adding IL-6. The ciliary neurotrophic factor, a member of the IL-6 superfamily, is neuroprotective for photoreceptors in retinal degeneration models and also for retinal ganglion cells in optic nerve damage models. The present study found high levels of IL-6 in the vitreous of patients with RD when compared to patients without RD, which suggests a neuroprotective effect. In addition, IL-6 levels are higher in detachments with longer evolution. These findings suggest that IL-6 plays a role in the protection of photoreceptors after neurosensory retina separation from the pigment epithelium. The therapeutic potential of IL-6 is endorsed by the evidence suggesting that high IL-6 levels in the vitreous humor has been documented in proliferative vitreoretinopathy, inflammation, retinal venous branch occlusion related to macular edema and the diabetic proliferative eye disease. In addition, IL-6 has been related to ocular neovascularization. However, it is not clear if high IL-6 levels in these conditions are the cause of the pathology or if IL-6 increases in response to the retinal disease. The data provided by the present study are convincing evidence of the increase of vitreous levels of IL-6 in the context of separation of neurosensory retina from RPE, suggesting that this could be a valuable point for therapeutic intervention to improve the visual results in patients with this type of retinal lesion.

Conflict of interest
No conflict of interests was declared by the authors.

REFERENCES

