Intravitreal autologous plasmin without associated-vitrectomy. Pharmacological vitreolysis, a perfeccionated method using urokinase

Dear Sir,

Pharmacological vitreolysis, also known as enzymatic vitrectomy utilizing autologous plasmin, has been utilized as coadjuvant during vitrectomy surgery to facilitate the peeling of the vitreoretinal interphase in pathologies such as macular hole, macular epiretinal membranes, proliferative vitreoretinopathy in the course of premature retinopathy, proliferative diabetic retinopathy and/or tractional retina detachment (1). One of the main problems for the use thereof was the sophisticated preparation technique, available only for top of the range hematological equipment.

Recently, several authors have published a simplified, simple, cheap and fast preparation method in the ophthalmology operating theatre immediately prior to the injection utilizing streptokinase as plasmin enzymatic activator (2,3). In addition, said technique is very efficient as a single intravitreal injection, without associating surgical vitrectomy, in diabetic macular edema as initial treatment as well as in cases which resist other therapies (laser, triamcinolone and intravitreous anti-Vegf) prior to deciding for surgical vitrectomy (Díaz-Llopis M et al, Intravitreal plasmin without associated-vitrectomy as a treatment for refractory diabetic macular edema. Eye 2008, in press). After having essayed said technique in over 30 cases with several pathologies, we have observed how the preparation of plasmin with streptokinase produces in all cases an initial loss of transparency of the vitreous, which is resolved within 1-7 days, with occasional intense post-injection uveitis cases.

We have developed an alternative method for preparing plasmin, substituting streptokinase by urokinase. The steps to be followed are: a) extraction of 7ml of blood from the patient in a coagulation tube, centrifuging it at 4,000 rpm for 15 minutes. At the same time a vial of urokinase (Urokinase Vedim®, 100,000 UI, Spain) is heated for 15 minutes at 37ºC. b) subsequently, 1.8 ml of plasma are mixed with 0.2 ml of urokinase, vigorously shaking the mixture an additional 2-3 minutes and maintaining it incubated at 37ºC up to time of use; c) sterilization of the solution with filtering through 0.22 micron Millipore filter, proceeding immediately to injection in the eye (0.2 ml) after generous anterior chamber paracentesis to avoid reflux.

By means of spectrophotometry at 405 nm of absorbance and utilizing the HD-NVA-CHA-lys-pN chromophoric agent, we have verified that the plasmin concentration is of 1.05 ± 0.12 UI/ml, very similar to that obtained with the streptokinase activation method (2,4), the injected amount —approximately 0.2 UI/0.2 ml— being well below toxic levels (3-4 UI) (1,2).

The plasmin urokinase preparation has the same clinical efficiency as plasmin streptokinase preparation and, with over 100 injections carried out, the main advantages of the former are an absolute absence of intraocular adverse inflammatory reactions and the lack of initial vitreous opacity. This allows for a perfect follow-up of the eye fundus from the time of the injection as well as a faster recovery from the transient vitreous haziness.

Fig. 1: A and B: Angiography image before and after plasmin treatment in a patient with diabetic macular edema. C and D: OCT image before and after intravitreal plasmin treatment in the same patient.
recovery and enhanced monitoring of the patient’s vision (fig. 1). Accordingly, we believe that the technique for preparing plasmin based on urokinase should be considered of choice, at least when utilized as the only intravitreous treatment —without associated surgical vitrectomy—.

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REFERENCES