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## Original article

# Treatment of vitreomacular traction syndrome with autologous plasmin enzyme<sup>☆</sup>



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### ABSTRACT

**Purpose:** To determine whether intravitreal injection of autologous plasmin enzyme (APE) is effective in vitreomacular traction syndrome (VMTS) by improving visual acuity and restoring macular morphology.

**Methods:** A prospective study of 11 consecutive patients diagnosed with VMTS in the Ophthalmology Department from January to May 2011. Inclusion criteria: best corrected visual acuity (BCVA) less than 0.5, and vitreomacular attachment in foveal area resulting in macular thickness >250 μm diagnosed by optical coherence tomography (Cirrus OCT, Carl Zeiss Meditec, Inc, Oberkochen, Germany). Exclusion criteria: active proliferative diabetic retinopathy, axial myopia >26 mm, vitrectomy, glaucoma, previous intravitreal injections and previous rhegmatogenous detachment. One to the 3 monthly intravitreal injections of 0.2 ml of APE was applied, interrupting if posterior vitreous detachment was attained. Wilcoxon's test was used for statistical analysis.

**Results:** A total of 12 eyes of 11 patients were treated. A complete posterior vitreous detachment was achieved in 4 (33%) eyes at the end of the study, 2 of them with one injection, and 2 with 3 monthly injections. Improvement of BCVA was statistically significant ( $p=0.017$ ) and the decrease in central macular thickness also was statistically significant ( $p=0.016$ ). There was only one complication: intraocular hypertension after injection that subsided with a new paracentesis.

**Conclusions:** Intravitreal APE injections avoided vitrectomy in VMTS in one in every 3 patients.

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## Tratamiento del síndrome de tracción vitreomacular con plasmina autógena

### R E S U M E N

#### Palabras clave:

Desprendimiento de vítreo  
Plasminógeno  
Vitreolisis  
Intraocular  
Inyecciones  
Edema macular

**Objetivo:** Analizar si la inyección intravítrea de plasmina autógena es eficaz en el síndrome de tracción vítreo-macular (STVM), mejorando la agudeza visual y restaurando la morfología macular.

**Métodos:** Estudio prospectivo de 11 pacientes consecutivos diagnosticados de STVM en nuestro Servicio de Oftalmología de enero a mayo de 2011. Criterios de inclusión: mejor agudeza visual corregida (MAVC) inferior a 0,5 y adhesión vítreo-macular foveal, ocasionando aumento del grosor macular central (GMC)  $> 250\mu$  diagnosticado mediante tomografía de coherencia óptica (Cirrus OCT, Carl Zeiss Meditec, Inc, Oberkochen, Alemania). Criterios de exclusión: retinopatía diabética proliferante activa, miopía axial  $> 26$  mm, vitrectomía previa, glaucoma, intravítreas previas y antecedentes de desprendimiento de retina. Se realizaron hasta 3 inyecciones mensuales de 0,2 ml de plasmina autógena, evaluándose a las 3 semanas de cada inyección el despegamiento de la adhesión vítreo-macular (AVM), MAVC, GMC y la recuperación de morfología macular en la OCT, interrumpiendo el tratamiento en caso de éxito. Análisis estadístico con test de Wilcoxon.

**Resultados:** De 12 ojos de 11 pacientes se consiguió despegamiento de AVM en 4 (33%), 2 con una inyección y 2 con 3 inyecciones. La mejoría de la MAVC ( $p=0,017$ ) y la disminución del GMC ( $p=0,016$ ) fueron estadísticamente significativas, mejorando la morfología macular en todos los casos con despegamiento de la AVM. La única complicación fue un caso de hipertensión intraocular tras la inyección, que cedió repitiendo la paracentesis.

**Conclusiones:** La inyección de plasmina autógena evitó la vitrectomía del STVM en uno de cada 3 pacientes.

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## Introduction

The vitreomacular traction syndrome (VMTS) is a disease caused by the partial detachment of the posterior hyaloids with persistence of macular adhesion. This vitreal-macular adhesion (VMA) could cause macular edema and macular cysts. The stage at which the external retina is involved by the traction is regarded as the initial stage of macular holes.<sup>1</sup> It is also been demonstrated that the release of VMA improves diabetic retinopathy edema.<sup>2</sup> At present, VMA release can only be achieved by vitrectomy with manual dissection of the posterior hyaloids. However, due to vitreous surgery risks, a few years ago surgeons began to try out intravitreal injection of substances to induce posterior hyaloids detachment, which produced promising results with plasmin<sup>3</sup> and microplasmin.<sup>4</sup>

Plasmin is a proteolytic enzyme obtained from plasminogen activation, utilizing a complex chromatography method or optionally in fresh human plasma by adding streptokinase or urokinase.<sup>5</sup> Microplasmin is a recombinant synthetic product with properties similar to human plasmin but considerably more stable. However, its preparation requires an experienced hematology team to carry out the complex process. Microplasmin has been used to facilitate mechanical vitrectomy in hyaloid traction of diabetic retinopathy<sup>6</sup> and in VMTS.<sup>7</sup> The efficacy of plasmin lies in its proteolytic effect which is free of retinal toxicity as it acts specifically on laminine and fibronectin present in the adhesion area, absolutely

respecting the internal limiting membrane due to its lack of activity on collagen type iv.<sup>8</sup>

A multicenter trial, presently in phase 2, is in course to assess treatment with microplasmin as initial therapy for VMTS.<sup>9</sup> The trial comprises 3 syndrome modes: idiopathic VMA, macular hole with traction and diabetic retinopathy tractional macular edema. In addition, the use of autogenic plasmin continues to be researched and the first results indicate that, if activated immediately prior to injection in the surgery, its results could be very similar to those of microplasmin<sup>10</sup> with the advantage that its preparation is easier and less expensive.

The present paper describes the initial results of treatment with autogenic plasmin in a group of patients with VMTS which is very similar to the group of the microplasmin multicenter trial. The main objective of this study is to determine whether autogenic plasmin is able to release VMA. The secondary objectives comprise the assessment of visual acuity evolution and macular thickness in these patients.

## Subjects, material and methods

A prospective intervention study in all consecutive patients diagnosed with VMTS in our Ophthalmology Department in its idiopathic, macular hole and tractional diabetes macular edema variants. The study was approved by the Ethical Research Committee of our hospital, which verified

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