Evaluation of rheopheresis in the treatment of non- exudative AMD

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Purpose:

Non-exudative age-related macular degeneration (AMD) is a cause of visual impairment for which the therapeutic arsenal is limited. Rheopheresis is an application of double filtration plasmapheresis specifically designed to treat microcirculatory disorders. Preliminary studies[1] demonstrated that treatment tended to reduce the number of drusen in AMD and reduce the frequency of neovascular complications. The objective of this study was to evaluate the effect of rheopheresis on the evolution of visual acuity, progression of atrophy and transition to exudative AMD over 24 months in non-exudative AMD.

Methods:

This prospective, randomized, controlled trial was conducted on patients with non-exudative AMD (stage 3 and 4) and was approved by the French ethics committee (ref 2006-A00671-50). All patient received AREDS-type vitamin supplementation. They were randomized into 2 groups: rheopheresis treatment or control. Patients were followed for two years. The parameters studied every six months were best-corrected visual acuity, retinal autofluorescence with area of atrophy measurement (Region Finder®) and central macular thickness on optical coherence tomography. Fluorescein angiography, central visual field and quality of life questionnaire "VQF 25" were evaluated at the beginning and end of the study. Blood biochemical tolerance was also monitored.

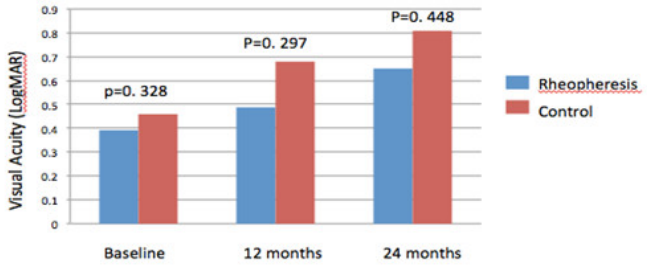
Results:

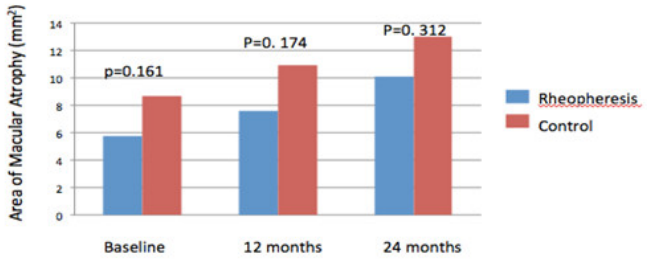
21 eyes of 21 patients (17 women, 4 men) with non-exudative AMD were followed from July 2009 to May 2013 (10 rheopheresis-treated and 11 controls). Unexpected problems in treatment availability resulted in a dramatic reduction in the number of enrolled patients. The average age of the patients was 78.3 ± 11.0 years for the rheopheresis group and 72.3 ± 8.2 years for the control group (p = .168).

For the rheopheresis and control groups respectively, visual acuity decreased from 0.39 and 0.46 logMAR at baseline (p= .328) to 0.49 and 0.68 logMAR at 12 months (p = .297) and to 0.65 and 0.81 logMAR at 24 months (p= .448).

The area of macular atrophy increased from 5.79 and 8.75 mm2 at baseline (p= .161) to 7.64 and 10.88 mm2 at 12 months (p= .174) and to 10.14 and 12.96 mm2 at 24 months (p= .312) for the rheopheresis and control group respectively.

The VQF25 score went from 75,63 and 74,3 (p= 0,708) at baseline to 71,63 and 73,6 (p= 0,536) at 24 months for the rheopheresis and control group respectively.

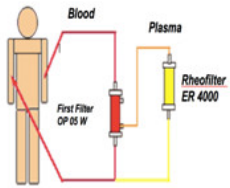




Mode of Action of Rheopheresis:

Rheopheresis is a plasmapheresis technique which selectively subtracts the high molecular weight macromolecules from the plasma via double filtration.
Rheopheresis decreases the concentration of large molecules in the plasma . For example, rheopheresis decreases serum cholesterol by 46% to 76% , LDL by 45% to 70%, alpha -2 macroglobulin by 50% to 70%, fibronectin by 43% , and fibrinogen by 40% to 67%. The decrease in the concentration of macromolecules is accompanied by a decrease in the plasma viscosity of about 10% to 15% and a decrease of about 45 % of erythrocyte aggregation through fibrinogen reduction .
Rheopheresis helps improve microcirculation.The utility of rheopheresis may arise from its action on viscosity, combined with its suppression of macromolecules playing a deleterious role in AMD.

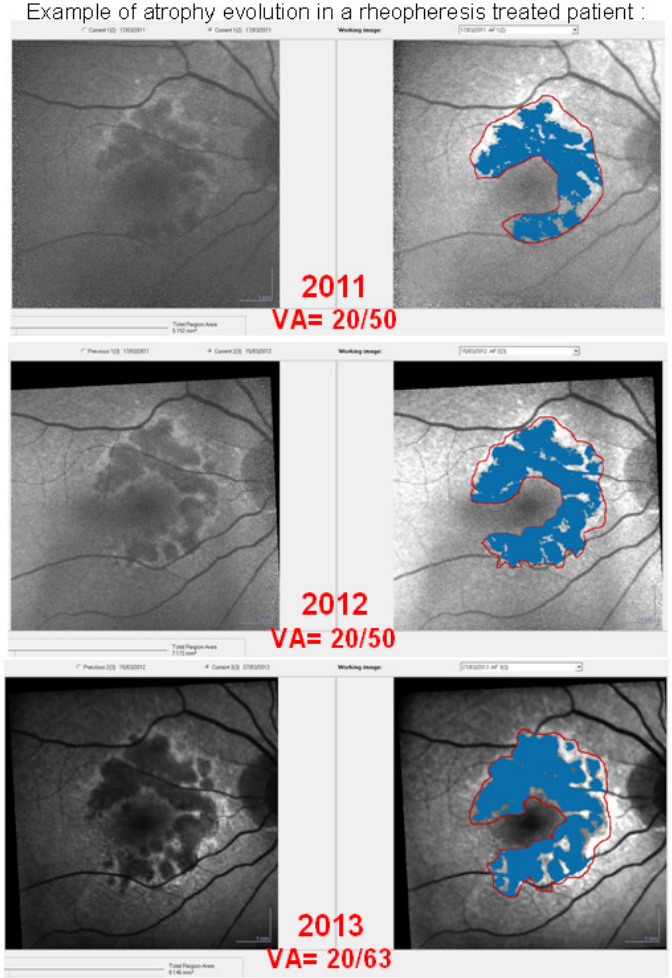
→ Legend: TT corresponds to Rheopheresis treatment sessions; a total of 8 sessions in 10 weeks.



→ Illustration showing the Rheopheresis double filtration process, to selectively reduce the plasma concentration of high molecular weight macromolecules.

Inclusion criteria	Exclusion criteria
Ophthalmologic inclusion criteria : - Visual acuity (VA) in the study eye of 20/32 to 20/63, - Study eye with atrophic AMD OR AMD risk stage 4, - Association of drusen> 125 µ and pigment migration OR presence of beaches of incipient atrophy with VA within limits, - Presence of more than medium-sized drusen (64µ) or 3 large drusen, - Association with a drusenoid DEP is possible, - Controlateral eye has an atrophic AMD with identical lesions as the first eye OR is lost for any other reason (can include monophtalmic patients), - Good access to the fundus in the studied eye, - Patient accepting the standard AREDS vitamin treatment (Preservision lutein 2cp/day), - Patient not taking other vitamin supplement.	**Ophthalmologic exclusion criteria :** - Other ophthalmological disease responsible for major decline in vision, - Exudative AMD in 1 of the 2 eyes, - Cataract surgery within the last 3 months - Cataract surgery scheduled in the next 24 months, - Unreliable measurement of VA or macular thickness, - Posterior capsular opacification of an intra-ocular implant (if pseudophakic patient).
General inclusion criteria : - 50 years of age or more, - If > 60 year-old: mandatory cardiology consultation (for rheopheresis patients), - Weight > 50 kg - Fibrinogen level ≥ 2.5 g /L, - Hematocrit ≥ 35%, - Patient informed about the objectives of the study - Consent of the patient, - Patient receiving social security.	**General exclusion criteria :** - Other ophthalmological disease responsible for major decline in vision, - Exudative AMD in 1 of the 2 eyes, - Cataract surgery within the last 3 months - Cataract surgery scheduled in the next 24 months, - Unreliable measurement of VA or macular thickness, - Posterior capsular opacification of an intra-ocular implant (if pseudophakic patient).

Example of atrophy evolution in a rheopheresis treated patient :



Conclusion:

Changes in visual acuity and in atrophic area were not statistically significant at 24 months between rheopheresis-treated patients and controls in non-exudative AMD. The study may have been insufficiently powered to detect a treatment difference. In this small series, rheopheresis did not seem to be effective in slowing the progression of atrophy in non-exudative AMD.

1. Pulido JS, Winters JL, Boyer D. Preliminary analysis of the final multicenter investigation of rheopheresis for age related macular degeneration (AMD) trial (MIRA-1) results. Trans Am Ophthalmol Soc. 2006;104:221-31.