

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "macular degeneration".

If you have not already subscribed, please email Rob Cummins at research@mdfoundation.com.au with 'Subscribe to MD Research News' in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your 'unsubscribe' request.

Drug treatment

Am J Ophthalmol. 2011 Nov 9. [Epub ahead of print]

Combined Intravitreal Ranibizumab and Photodynamic Therapy for Retinal Angiomatous Proliferation.

Saito M, Iida T, Kano M.

Department of Ophthalmology, Fukushima Medical University School of Medicine, Fukushima, Japan.

PURPOSE: To clarify the efficacy of combined therapy with intravitreal ranibizumab injections and photodynamic therapy (PDT) in patients with symptomatic retinal angiomatous proliferation.

DESIGN: Retrospective, interventional, consecutive case series.

METHODS: We retrospectively reviewed 20 treatment-naïve eyes of 16 patients (8 men, 8 women; age range, 79 to 92 years; mean age, 84.8 years) treated with 3 consecutive monthly intravitreal injections of ranibizumab (0.5 mg/0.05 mL) and PDT and followed up for at least 12 months. PDT was applied 1 or 2 days after the initial injection. Retreatment was performed as a combined therapy of a single intravitreal ranibizumab injection and PDT.

RESULTS: The mean best-corrected visual acuity (BCVA) levels significantly improved from 0.24 at baseline to 0.43 at 12 months ($P < .001$). The mean improvement in BCVA at 12 months from baseline was 2.51 lines. The BCVA at 12 months improved in 10 eyes (improved by 3 lines or more) and was stable (defined as a loss of less than 3 lines of vision) in 10 eyes. No patient had a decrease in the BCVA of 3 lines or more during any 12 months. The central retinal thickness decreased significantly from 444 μm at baseline to 143 μm at 12 months ($P < .0001$). Complete occlusion of the retinal-retinal anastomosis was achieved in 17 of the 19 eyes at 12 months. The mean numbers of PDT treatments and injections during 12 months, including the treatments in the initial regimen, were 1.8 and 3.8, respectively. No complications or systemic adverse events developed.

CONCLUSIONS: Combined intravitreal ranibizumab and PDT for patients with retinal angiomatous proliferation effectively maintained or improved visual acuity and reduced the exudation without adverse events.

PMID:22078902 [PubMed - as supplied by publisher]

Retina. 2011 Nov 11. [Epub ahead of print]

FACTORS AFFECTING PATIENTS' PAIN INTENSITY DURING IN OFFICE INTRAVITREAL INJECTION PROCEDURE.

Rifkin L, Schaal S.

From the Department of Ophthalmology and Visual Sciences University of Louisville, Louisville, Kentucky.

PURPOSE: To determine factors associated with patients' comfort during routine in-office intravitreal injection.

METHODS: Sixty patients receiving intravitreal injections over 15 months for macular edema because of diabetes, age-related macular degeneration, or retinal vein occlusion who were randomized into 3 groups to receive 1 of 3 commonly used forms of anesthesia-TetraVisc, proparacaine HCl, or tetracaine HCl-before receiving intravitreal injection were studied. Fifteen minutes after injection, patients were asked to rate their pain from 0 (no pain/no distress) to 10 (agonizing pain/unbearable distress) using a Visual Analog Pain score survey. Self-reported pain scores were stratified by age, gender, diagnosis, injection number, substance injected, needle gauge, and visual acuity improvement.

RESULTS: Intravitreal injection was associated with low pain scores. Patients receiving tetracaine reported a statistically significant lower pain score (3.05 ± 2.01) than patients receiving proparacaine (3.17 ± 2.18) or TetraVisc (3.39 ± 2.26 ; $P < 0.01$). Other important factors influencing pain score significantly ($P < 0.01$) included improved vision from previous injection, female sex, and age >65 years. Pain scores decreased with each consecutive injection.

CONCLUSION: Pain associated with intravitreal injection is generally mild, and may be associated with epidemiologic and environmental factors.

PMID:22082694 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2011 Nov 14. [Epub ahead of print]

[Efficacy of intravitreal injections of ranibizumab compared to visudyne phototherapy in myopic choroidal neovascularization associated with high myopia.]

[Article in French]

Dethorey G, Leveziel N, Lalloum F, Forte R, Guigui B, Querques G, Glacet-Bernard A, Soubrane G, Souied HE.

Département d'ophtalmologie, centre hospitalier intercommunal de Créteil, 40, avenue de Verdun, 94000 Créteil, France.

INTRODUCTION: Myopic choroidal neovascularization (CNV) is the first cause of CNV in young patients. The aim of this study was to compare the efficacy of intravitreal injections (IVT) of ranibizumab with photodynamic therapy (PDT) in this indication.

PATIENTS AND METHODS: Retrospective comparative study analyzing the visual acuity (VA) outcomes of CNV myopic patients treated with either IVT or PDT.

RESULTS: Twenty-seven eyes of 25 patients were treated with PDT (group 1) and 18 eyes of 17 patients were treated with IVT of ranibizumab (group 2). Demographic data were similar in the two groups. The median initial VA was 20/80 for group 1 and 20/160 for group 2 ($P=0.37$). At 1 year, the median VA was 20/80 for group 1 ($P=0.32$) and 20/63 for group 2 ($P=0.04$). A significant improvement in VA was observed in 23.1% and in 27.3% of cases in groups 1 and 2, respectively ($P=0.53$). A significant VA worsening was observed in 34.6% of cases in group 1 and in 9.1% of cases in group 2 ($P=0.21$).

CONCLUSION: IVT of ranibizumab compared to PDT treatment showed greater efficacy in this study.

PMID:22088356 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Arch Ophthalmol. 2011 Nov;129(11):1466-74.

Aceruloplasminemia: retinal histopathologic manifestations and iron-mediated melanosome degradation.

Wolkow N, Song Y, Wu TD, Qian J, Guerquin-Kern JL, Dunaief JL.

F. M. Kirby Center for Molecular Ophthalmology, Scheie Eye Institute, Perelman School of Medicine, University of Pennsylvania, 305 Stellar Chance Labs, 422 Curie Blvd, Philadelphia, PA 19104.
jdunaief@mail.med.upenn.edu.

OBJECTIVE: To examine the retinal histopathologic manifestation of aceruloplasminemia, an autosomal recessive disease caused by mutation of the ferroxidase ceruloplasmin, resulting in tissue iron overload.

METHODS: The morphologic features of the human aceruloplasminemic retina were studied with light and electron microscopy. Retinal iron accumulation was assessed with Perls Prussian blue staining, immunohistochemistry, and secondary ion mass spectrometry.

RESULTS: Light and electron microscopic analysis revealed several ocular pathologic findings that resembled age-related macular degeneration, including retinal pigment epithelium (RPE) depigmentation, atrophy and hypertrophy, nodular and diffuse drusen, and lipofuscin and melanolipofuscin granules. Complement deposition was detected in drusen. The RPE cells and neural retina had increased levels of iron. Two major types of RPE cells were observed: melanosome rich and melanosome poor. Melanosome-rich cells had increased levels of iron and melanolipofuscin. The melanolipofuscin granules were observed in large aggregates, where some of the melanosomes were degrading. Melanosome-poor cells lacked melanosomes, melanolipofuscin, and lipofuscin but contained electron-dense aggregates high in iron, phosphorus, and sulfur.

CONCLUSIONS: The findings in the aceruloplasminemic retina resemble some of those found in age-related macular degeneration. Also, they suggest that melanosomes in the RPE can be degraded via iron-mediated reactive oxygen species production. **Clinical Relevance** Mechanisms underlying the pathologic mechanisms found in aceruloplasminemia also may be important in age-related macular degeneration.

PMID:22084216 [PubMed - in process]

Int Ophthalmol. 2011 Nov 11. [Epub ahead of print]

Color vision in an elderly patient with protanopic genotype and successfully treated unilateral age-related macular degeneration.

Kitakawa T, Hayashi T, Tsuzuranuki S, Kubo A, Tsuneoka H.

Department of Ophthalmology, The Jikei University School of Medicine, 3-25-8, Nishi-shimbashi, Minato-ku, Tokyo, 105-8461, Japan.

Abstract

We investigated differences in color discrimination between the fellow eye and the affected eye successfully treated for unilateral age-related macular degeneration (AMD) in a 69-year-old male patient with protanopia. His best-corrected visual acuity (BCVA) was 1.2 in the right eye (RE) and 0.2 in the left eye (LE). Fundus and angiographic findings showed classic choroidal neovascularization (CNV) secondary to AMD in the LE. BCVA of the LE improved to 0.4, and CNV resolved by 15 months after initiating combined anti-vascular endothelial growth factor and photodynamic therapies. After CNV closure, the Farnsworth dichotomous was performed, showing confusion patterns of the protan axis in either eye. The Farnsworth-Munsell 100-hue test showed a total error score of 520 in the LE, much higher than the score of 348 in the RE. Complete genotypes of the long-wavelength-sensitive (L-) cone and middle-wavelength-sensitive (M-) cone opsin genes were determined by polymerase chain reaction, revealing that the patient had a single 5' L-M 3' hybrid gene (encoding an M-cone opsin), with this genotype responsible for protanopia (the L-cone

opsin gene was non-functional), instead of the L-cone and M-cone opsin gene arrays. Poorer color vision discrimination in the LE than the RE remained present despite closure of CNV. The presence and type of congenital color vision defect can be confirmed using molecular genetic testing even if complications of acquired retinal diseases such as AMD are identified.

PMID:22076412[PubMed - as supplied by publisher]

Pathogenesis

Retina. 2011 Nov 15. [Epub ahead of print]

THE EFFECT OF NICOTINE ON ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY IN A MOUSE MODEL OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Davis SJ, Lyzogubov VV, Tytarenko RG, Safar AN, Bora NS, Bora PS.

Department of Ophthalmology, Jones Eye Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas.

PURPOSE: The purpose of this article is to evaluate the effect of nicotine on anti-vascular endothelial growth factor therapy in the treatment of neovascular age-related macular degeneration.

METHODS: One group of mice received nicotine in drinking water and the other group received water only. Choroidal neovascularization (CNV) was induced with a laser. Nicotinic acetylcholine receptor- $\alpha 7$ (nAChR $\alpha 7$) expression was evaluated by immunohistochemistry. Bevacizumab or adiponectin peptide II (APNpII) was injected intravitreally on Day 7 postlaser, and the effects were evaluated on Days 14 and 21. α -Bungarotoxin was injected intraperitoneally on Days 2 to 5, and its effect was evaluated on Day 14.

RESULTS: Expression of nAChR $\alpha 7$ was 2 to 7 times higher between Days 3 and 7 postlaser compared with naive mice. In water-fed mice, APNpII, bevacizumab, and α -bungarotoxin significantly reduced CNV size. In nicotine-fed mice, treatment with APNpII or bevacizumab did not significantly reduce CNV size, whereas α -bungarotoxin did have an effect. Comparing water- and nicotine-fed mice, CNV size was 61% to 86% smaller in water-fed mice except for the α -bungarotoxin group, where there was no difference. Platelet-derived growth factor and vascular endothelial growth factor expression was 1.5- to 2.5-fold higher at Day 14 in nicotine-treated mice.

CONCLUSION: Nicotine significantly blocks the effect of anti-vascular endothelial growth factor therapy in the treatment of laser-induced neovascular age-related macular degeneration. nAChR $\alpha 7$ is significantly upregulated during the formation of CNV, and treatment with an nAChR $\alpha 7$ antagonist decreases CNV size irrespective of nicotine administration.

PMID:22088983 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2011 Nov 13. [Epub ahead of print]

Proteomic profiling of human retinal pigment epithelium exposed to an advanced glycation-modified substrate.

Glenn JV, Mahaffy H, Dasari S, Oliver M, Chen M, Boulton ME, Xu H, Curry WJ, Stitt AW.

School of Medicine, Dentistry and Biomedical Science, Queen's University Belfast, Northern Ireland, UK.

PURPOSE: The retinal pigment epithelium (RPE) and underlying Bruch's membrane undergo significant modulation during ageing. Progressive, age-related modifications of lipids and proteins by advanced glycation end products (AGEs) at this cell-substrate interface have been implicated in RPE dysfunction and the progression to age-related macular degeneration (AMD). The pathogenic nature of these adducts in Bruch's membrane and their influence on the overlying RPE remains unclear. This study aimed to identify alterations in RPE protein expression in cells exposed to AGE-modified basement membrane (AGE-BM), to determine how this "aged" substrate impacts RPE function and to map the localisation of identified proteins

in ageing retina.

METHODS: Confluent ARPE-19 monolayers were cultured on AGE-BM and native, non-modified BM (BM). Following 28-day incubation, the proteome was profiled using 2-dimensional gel electrophoresis (2D), densitometry and image analysis was employed to map proteins of interest that were identified by electrospray ionisation mass spectrometry (ESI MS/MS). Immunocytochemistry was employed to localise identified proteins in ARPE-19 monolayers cultured on unmodified and AGE-BM and to analyze aged human retina.

RESULTS: Image analysis detected altered protein spot densities between treatment groups, and proteins of interest were identified by LC ESI MS/MS which included heat-shock proteins, cytoskeletal and metabolic regulators. Immunocytochemistry revealed deubiquitinating enzyme ubiquitin carboxyterminal hydrolase-1 (UCH-L1), which was upregulated in AGE-exposed RPE and was also localised to RPE in human retinal sections.

CONCLUSIONS: This study has demonstrated that AGE-modification of basement membrane alters the RPE proteome. Many proteins are changed in this ageing model, including UCHL-1, which could impact upon RPE degradative capacity. Accumulation of AGEs at Bruch's membrane could play a significant role in age-related dysfunction of the RPE.

PMID:22081232 [PubMed - as supplied by publisher]

Disclaimer: This newsletter is provided as a free service to eye care professionals by the Macular Degeneration Foundation. The Macular Degeneration Foundation cannot be liable for any error or omission in this publication and makes no warranty of any kind, either expressed or implied in relation to this publication.