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MD Research News

Issue 17

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Drug Treatment

Surv Ophthalmol. 2011 Mar-Apr;56(2):95-113.

Systemic and Ocular Safety of Intravitreal Anti-VEGF Therapies for Ocular Neovascular Disease.

Tolentino M.

Center for Retina & Macular Disease, Winter Haven, Florida, USA.

Abstract

The treatment of ocular neovascular diseases is being revolutionized by intravitreal therapies targeting vascular endothelial growth factor (VEGF). Two agents are approved for treating neovascular age-related macular degeneration and are being evaluated for other retinal conditions: the RNA aptamer pegaptanib and the monoclonal antibody antigen-binding fragment ranibizumab. Bevacizumab, a related antibody, is being used similarly, although its use is off-label. Pegaptanib selectively binds to a VEGF isoform identified as being especially pathogenic in the eye and spares other isoforms, whereas the other two agents nonselectively bind all VEGF isoforms. Because VEGF is involved in a wide variety of physiologic processes, the ocular and systemic safety of anti-VEGF agents is of paramount concern. I provide an overview of safety data for intravitreal anti-VEGF therapies, focusing primarily on randomized, controlled trials. For pegaptanib, an accumulation of data from pivotal trials and a dedicated systemic safety study have revealed no ocular or systemic safety concerns. For ranibizumab, the principal ocular adverse event detected in clinical trials was a low frequency of ocular inflammation, and systemic adverse events included a slightly elevated risk of nonocular hemorrhage and stroke. Safety data from properly designed randomized controlled trials for bevacizumab are not available.

PMID: 21335144 [PubMed - in process]

Ophthalmologica. 2011 Feb 18;225(4):211-221. [Epub ahead of print]

Arterial Thromboembolic Events in Patients with Exudative Age-Related Macular Degeneration Treated with Intravitreal Bevacizumab or Ranibizumab.

Carneiro AM, Barthelmes D, Falcão MS, Mendonça LS, Fonseca SL, Gonçalves RM, Faria-Correia F, Falcão-Reis FM.

Department of Ophthalmology, Hospital São João, University of Porto, Porto, Portugal.

Background/Aims: To compare retrospectively the incidence of arterial thromboembolic events (ATEs) in patients treated with bevacizumab or ranibizumab for exudative age-related macular degeneration.

Methods: Charts of 378 patients treated with at least 1 intravitreal injection of ranibizumab or bevacizumab were reviewed to calculate the incidence of ATEs. Only patients under monotherapy were analyzed.

Results: ATEs occurred in 15 patients: 12 (12/97) with bevacizumab (12.4%) and 3 (3/219) with ranibizumab (1.4%) - odds ratio 10.16; 95% confidence interval 2.80-36.93; $p < 0.0001$. ATEs in the bevacizumab and ranibizumab cohorts included stroke, myocardial infarction, angina pectoris, peripheral thromboembolic disease, transient ischemic attack, sudden death and lethal stroke.

Conclusion: In this series, bevacizumab raised the risk of ATEs when compared to ranibizumab. In an elderly population with multiple cardiovascular risk factors, the new ATEs may not be attributed exclusively to the intravitreal bevacizumab administration. These findings raise an issue that must be confirmed in randomized clinical trials.

PMID: 21336001 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2011 Feb 18. [Epub ahead of print]

Monthly Ranibizumab for Nonproliferative Macular Telangiectasia Type 2: A 12-Month Prospective Study.

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Department of Ophthalmology, University of Bonn, Bonn, Germany; Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, United Kingdom.

PURPOSE: To investigate the efficacy and safety of intravitreal ranibizumab for the treatment of nonproliferative macular telangiectasia (MacTel) type 2.

DESIGN: Prospective, open-label, uncontrolled, nonrandomized interventional clinical trial.

METHODS: One eye (disease stage 2 or 3) of each patient (n = 10) with nonproliferative MacTel type 2 was injected with 0.5 mg ranibizumab at monthly intervals for one year. Visual acuity, angiographic findings, and retinal thickness were assessed at each visit. The primary endpoint was the change in best-corrected distance visual acuity after one year compared to baseline.

RESULTS: Mean visual acuity showed a transient increase in the study eye. However, after 12 months of treatment there was no significant change of visual acuity compared to baseline or compared to the fellow eye. Fluorescein angiography revealed a decrease of telangiectatic-appearing capillaries and of late-phase leakage, which was accompanied by a topographically related significant reduction in macular thickness. Three to 5 months after the last treatment, angiographic appearance and retinal thickness were similar to baseline. In one patient, the last intravitreal injection was not performed because of safety concerns after a transitory ischemic attack. Otherwise, no serious adverse events were observed.

CONCLUSIONS: The angiographic and tomographic effects after intravitreal inhibition of vascular endothelial growth factor (VEGF) using ranibizumab implicate a pathophysiological role of the VEGF pathway in nonproliferative MacTel type 2. As the morphologic response was not associated with a clear functional benefit, and because of the transient nature of the treatment effect, monthly intravitreal ranibizumab is not recommended for the nonproliferative disease stage of MacTel type 2.

PMID: 21334595 [PubMed - as supplied by publisher]

Med Clin (Barc). 2011 Feb 21. [Epub ahead of print]

[Assessment of the effectiveness and safety of ranibizumab in neovascular age-related macular degeneration.]

[Article in Spanish]

Real Campaña JM, Carrera Lafuentes P, Torrón Fernández-Blanco C, Huarte Lacunza R, Varela Martínez I, Rabanaque Hernández MJ.

Servicio de Farmacia, Hospital Universitario Miguel Servet, Zaragoza, España.

BACKGROUND AND OBJECTIVES: Neovascular Age Related Macular Degeneration (ARMD) is a chronic and degenerative disease. Current treatment options are limited and have shown to slow disease progression. The aim of this study was to assess Ranibizumab effectiveness and safety and to describe patients' demographic and clinical characteristics.

PATIENTS AND METHOD: We conducted a retrospective observational study including all patients who had started treatment between 1/12/2006 and 31/12/2008, and were followed up until 31/03/2009. A bivariate analysis on months 4, 12 and 18 and two logistic regression models were performed to analyze the influence of demographic and clinical factors on the effectiveness and durability of treatment. Adverse reactions were collected as described in the medical records to assess safety.

RESULTS: A total of 126 eyes of 112 patients were recruited. The mean age was 77.7 (± 6.0) years. The mean durability of treatment was 18.2 months, and it was higher in the group of patients who started treatment with visual acuity (VA) > 0.1 (p<0.001). Ranibizumab therapy maintained AV over baseline at 18 months. None of the studied variables showed any influence on treatment effectiveness. However, baseline visual acuity influenced on treatment duration, being higher in the group of patients with AV > 0.1.

CONCLUSIONS: Ranibizumab was shown to be effective until 18 months. Early diagnosis of AMD could lead to an earlier treatment start, when patients present a higher AV, in order to optimize the benefits of treatment. Ranibizumab was well tolerated and safe in most patients.

PMID: 21345465 [PubMed - as supplied by publisher]

Retina. 2011 Mar;31(3):446-52.

A retrospective analysis of triple combination therapy with intravitreal bevacizumab, posterior sub-tenon's triamcinolone acetonide, and low-fluence verteporfin photodynamic therapy in patients with neovascular age-related macular degeneration.

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PURPOSE: : To assess the efficacy of triple combination therapy (TCT) including bevacizumab (BEV), low-fluence photodynamic therapy, and posterior sub-Tenon's triamcinolone acetonide in patients with wet age-related macular degeneration.

METHODS: : This institutional review board-approved retrospective consecutive case series included 31 eyes treated for wet age-related macular degeneration with TCT at the Beth Israel Deaconess Medical Center between June 2004 and November 2008. Outcome measures included visual acuity, retinal thickness as measured by optical coherence tomography, time to retreatment, and complications.

RESULTS: : Triple combination therapy eyes showed significant 3-month and 6-month improvement in visual acuity of 0.140 ± 0.273 logarithm of the minimum angle of resolution and 0.182 ± 0.383 logarithm of the minimum angle of resolution after treatment, respectively (P = 0.0219 and 0.0470, respectively). Central retinal thickness significantly improved at 3 months (-123.8 ± 102.7 μm), 6 months (-87.7 ± 99.8 μm), and 12 months (-101.6 ± 103.3 μm) on optical coherence tomography. Half of eyes that underwent TCT required retreatment by the conclusion of their follow-up, and eyes that underwent TCT had a 1-year Kaplan-Meier survival rate of 62.1 ± 10.8%.

CONCLUSION: : Triple combination therapy (TCT) appears to effectively improve visual acuity and decrease retinal thickness often without need for subsequent retreatment within the first year of follow-up. Further investigation of TCT in prospective trials is warranted.

PMID: 21336068 [PubMed - in process]

Expert Opin Drug Deliv. 2011 Feb 22. [Epub ahead of print]

Drug delivery strategies for therapeutic angiogenesis and antiangiogenesis.

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Abstract

Introduction: Angiogenesis is essential to human biology and of great clinical significance. Excessive or reduced angiogenesis can result in, or exacerbate, several disease states, including tumor formation, exudative age-related macular degeneration (AMD) and ischemia. Innovative drug delivery systems can increase the effectiveness of therapies used to treat angiogenesis-related diseases. Areas covered: This paper reviews the basic biology of angiogenesis, including current knowledge about its disruption in diseases, with the focus on cancer and AMD. Anti- and proangiogenic drugs available for clinical use or in development are also discussed, as well as experimental drug delivery systems that can potentially improve these therapies to enhance or reduce angiogenesis in a more controlled manner. Expert opinion: Laboratory and clinical results have shown pro- or antiangiogenic drug delivery strategies to be effective in drastically slowing disease progression. Further research in this area will increase the efficacy, specificity and duration of these therapies. Future directions with composite drug delivery systems may make possible targeting of multiple factors for synergistic effects.

PMID: 21338327 [PubMed - as supplied by publisher]

Eye (Lond). 2011 Feb 25. [Epub ahead of print]

Comment on 'Bevacizumab vs ranibizumab for age-related macular degeneration: 1-year outcomes of a prospective, double-masked randomised clinical trial'

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PMID: 21350573 [PubMed - as supplied by publisher]

Eye (Lond). 2011 Feb 25. [Epub ahead of print]

Response to comment on 'Bevacizumab vs ranibizumab for age-related macular degeneration: 1-year outcomes of a prospective, double-masked randomised clinical trial'

Subramanian ML.

Department of Ophthalmology, Boston University School of Medicine and the VA Boston Healthcare System, Boston, MA, USA.

PMID: 21350574 [PubMed - as supplied by publisher]

CMAJ. 2011 Feb 22. [Epub ahead of print]

Ranibizumab and the eye.

Noble J, Chaudhary V.

PMID: 21343272 [PubMed - as supplied by publisher]

Harv Health Lett. 2011 Jan;36(3):7.

Good news about new macular degeneration drugs.

[No authors listed]

PMID: 21341413 [PubMed - in process]

Indian J Ophthalmol. 2011 Mar-Apr;59(2):145-8.

Flare up of choroiditis and choroidal neovasculazation associated with punctate inner choroidopathy during early pregnancy.

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Uveitis Services, Shri Ganapati Netralaya, Jalna, Maharashtra, India.

Abstract

A 28-year-old, healthy female, who had a recent repeated history of miscarriage, presented with bilateral choroidal neovascular membranes (CNVM), for which she received photodynamic therapy with three doses of lucentis, at intervals of one month each, to which she responded. After five months, the patient again presented with complaints of diminution of vision since 15 days. She had a history of miscarriage two days before presenting to our clinic. CNVM was scarred at this time and the fundus picture showed multiple small punctate spots around the fovea at the level of the choroid, which showed early hyperfluroscence on fundus fluorescein angiography, suggestive of punctate inner choroidopathy. She was advised systemic steroids, to which she responded dramatically.

PMID: 21350285 [PubMed - in process]

Other treatment & diagnosis

Acta Ophthalmol. 2011 Feb 18. doi: 10.1111/j.1755-3768.2011.02123.x. [Epub ahead of print]

Drusen detection in retro-mode imaging by a scanning laser ophthalmoscope.

Acton JH, Cubbidge RP, King H, Galsworthy P, Gibson JM.

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Purpose: The Nidek F-10 is a scanning laser ophthalmoscope that is capable of a novel fundus imaging technique, so-called 'retro-mode' imaging. The standard method of imaging drusen in age-related macular degeneration (AMD) is by fundus photography. The aim of the study was to assess drusen quantification using retro-mode imaging.

Methods: Stereoscopic fundus photographs and retro-mode images were captured in 31 eyes of 20 patients with varying stages of AMD. Two experienced masked retinal graders independently assessed images for the number and size of drusen, using purpose-designed software. Drusen were further assessed in a subset of eight patients using optical coherence tomography (OCT) imaging.

Results: Drusen observed by fundus photography (mean 33.5) were significantly fewer in number than subretinal deposits seen in retro-mode (mean 81.6; $p < 0.001$). The predominant deposit diameter was on average 5 μm smaller in retro-mode imaging than in fundus photography ($p = 0.004$). Agreement between graders for both types of imaging was substantial for number of deposits (weighted $\kappa = 0.69$) and moderate for size of deposits (weighted $\kappa = 0.42$). Retro-mode deposits corresponded to drusen on OCT imaging in all eight patients.

Conclusion: The subretinal deposits detected by retro-mode imaging were consistent with the appearance of drusen on OCT imaging; however, a larger longitudinal study would be required to confirm this finding. Retro-mode imaging detected significantly more deposits than conventional colour fundus photography. Retro-mode imaging provides a rapid non-invasive technique, useful in monitoring subtle changes and progression of AMD, which may be useful in monitoring the response of drusen to future therapeutic interventions.

PMID: 21332676 [PubMed - as supplied by publisher]

Photodiagnosis Photodyn Ther. 2011 Mar;8(1):14-29. Epub 2010 Dec 28.

Nanodrug applications in photodynamic therapy.

Paszko E, Ehrhardt C, Senge MO, Kelleher DP, Reynolds JV.

Medicinal Chemistry, Institute of Molecular Medicine, Trinity Centre for Health Sciences, Trinity College Dublin, St James's Hospital, Dublin 8, Ireland.

Abstract

Photodynamic therapy (PDT) has developed over last century and is now becoming a more widely used medical tool having gained regulatory approval for the treatment of various diseases such as cancer and macular degeneration. It is a two-step technique in which the delivery of a photosensitizing drug is followed by the irradiation of light. Activated photosensitizers transfer energy to molecular oxygen which results in the generation of reactive oxygen species which in turn cause cells apoptosis or necrosis. Although this modality has significantly improved the quality of life and survival time for many cancer patients it still offers significant potential for further improvement. In addition to the development of new PDT drugs, the use of nanosized carriers for photosensitizers is a promising approach which might improve the efficiency of photodynamic activity and which can overcome many side effects associated with classic photodynamic therapy. This review aims at highlighting the different types of nanomedical approaches currently used in PDT and outlines future trends and limitations of nanodelivery of photosensitizers.

PMID: 21333931 [PubMed - in process]

Manag Care. 2010 Dec;19(12):47-8.

Telescope placed in eye improves central vision.

Morrow T.

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PMID: 21291134 [PubMed - indexed for MEDLINE]

Vision Res. 2011 Feb 15. [Epub ahead of print]

Gaze-contingent simulation of retinopathy: Some potential pitfalls and remedies.

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Abstract

Many important results in visual neuroscience rely on the use of gaze-contingent retinal stabilization techniques. Our work focuses on the important fraction of these studies that is concerned with the retinal stabilization of visual filters that degrade some specific portions of the visual field. For instance, macular scotomas, often induced by Age Related Macular Degeneration, can be simulated by continuously displaying a gaze-contingent mask in the center of the visual field. The gaze-contingent rules used in most of these studies imply only a very minimal processing of ocular data. By analyzing the relationship between gaze and scotoma locations for different oculo-motor patterns, we show that such a minimal processing might have adverse perceptual and oculomotor consequences due mainly to two potential problems: a/ a transient blink-induced motion of the scotoma while gaze is static, and b/ the intrusion of post-saccadic slow eye movements. We have developed new gaze-contingent rules to solve these two problems. We have also suggested simple ways of tackling two unrecognized problems that are a potential source of mismatch between gaze and scotoma locations. Overall, the present work should help design, describe and test the paradigms used to simulate retinopathy with gaze-contingent displays.

PMID: 21335024 [PubMed - as supplied by publisher]

Retina. 2011 Mar;31(3):553-8.

Morphologic differences, according to etiology, in pigment epithelial detachments by means of en face optical coherence tomography.

Lumbroso B, Savastano MC, Rispoli M, Balestrazzi A, Savastano A, Balestrazzi E.

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PURPOSE: : To assess morphologic differences in pigment epithelial detachment (PED) with en face optical coherence tomography in central serous chorioretinopathy (CSC) and age-related macular degeneration (AMD).

METHODS: : We recruited 30 eyes of 22 patients with PED. Nine eyes had a clinical diagnosis of CSC and 21 had AMD. All patients were assessed with en face optical coherence tomography. Morphologic PED aspects were estimated on C-scans and classified according to shape, inner silhouette, content, wall aspects, wall thickness, and size.

RESULTS: : Pigment epithelial detachment shape was predominantly circular (88.8%) in CSC and irregular or with multilobular features in AMD (76.2%). The PED inner silhouette had a smooth aspect (88.9%) in CSC and a slightly granular aspect or granular profile in AMD (100%). Clear PED content was the most characteristic feature of CSC (88.9%) but not of AMD. In CSC, PED morphologic wall aspect was uniform or slightly irregular (100%), while in AMD, it was slightly irregular (52.4%) or irregular (47.6%). Pigment epithelial detachment wall thickness and dimensions were larger in AMD than in CSC. Statistically significant differences were observed between CSC and AMD concerning PED inner silhouette, contents, wall aspects, and wall thickness measurements.

CONCLUSION: : En face optical coherence tomography scanning is a valuable tool for showing important morphologic differences between CSC and AMD.

PMID: 21343873 [PubMed - in process]

Br J Ophthalmol. 2011 Feb 24. [Epub ahead of print]

Conversion of Stratus optical coherence tomography (OCT) retinal thickness to Cirrus OCT values in age-related macular degeneration.

Krebs I, Hagen S, Smretschnig E, Womastek I, Brannath W, Binder S.

Vienna, Austria.

Aim: Spectral domain optical coherence tomography (SD OCT) is of increasing importance and is gradually replacing time domain OCT (TD OCT). Our aim was to determine a formula to convert Stratus OCT (TD OCT) to Cirrus OCT (SD OCT) retinal thickness.

Methods: Central retinal thickness (CRT) and retinal volume (RV) were obtained by the macular thickness program of Stratus OCT and the cube 512×128 program of Cirrus OCT in patients with exudative age-related macular degeneration (AMD). Algorithm line failures were corrected. A linear model with Stratus OCT CRT as fixed factor and Cirrus OCT CRT as dependent variable was applied to calculate the conversion formula.

Results: OCT examinations of 104 eyes of 104 patients were reviewed and corrected when necessary. Stratus and Cirrus OCT CRT were significantly correlated ($p<0.0001$). For CRT the formula Cirrus CRT=58.63+0.94× Stratus CRT was calculated. The correlation was significantly influenced by the height of the CRT values ($p<0.0001$), but not by whether correction was necessary. For RV the formula Cirrus OCT RV=3.098+0.98× Stratus OCT RV was calculated.

Conclusion: Stratus OCT and Cirrus OCT use a different posterior reference line within the hyper-reflective band of the outer retina. Therefore a conversion formula is necessary to compare Stratus and Cirrus OCT CRT values, and this has been determined in our study.

PMID: 21349936 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2011 Feb 18. doi: 10.1111/j.1755-3768.2011.02115.x. [Epub ahead of print]

Intravitreal recombinant tissue plasminogen activator without and with additional gas injection in patients with submacular haemorrhage associated with age-related macular degeneration.

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University Eye Hospital, University Clinics Muenster, Muenster, Germany.

Purpose: To compare intravitreal recombinant tissue plasminogen activator (rt-PA) treatment with and without gas injection in patients with submacular haemorrhage associated with age-related macular degeneration.

Methods: We conducted a retrospective, non-randomized comparative case study of 110 eyes from 76 women and 34 men (mean age 78.1 ± 6.9 years). Evaluations of the data were performed for baseline visit (t1), and visits 1-3 weeks (t2), 3 months (t3) and 6 months after (t4). The patients were classified according to gas treatment into group A (without gas, n = 46) and group B (with gas, n = 64) and according to rt-PA-dosage into group A1 and B1 (50 µg), group A2 and B2 (100 µg), and group A3 and B3 (200 µg).

Results: At t4, the patients in group A had a median increase of 0.4 logMAR, and those in group B had a

decrease of 0.1 logMAR (p = 0.183). The best corrected visual acuity (BCVA) remained stable or increased in 55% and 62% of patients in groups A and B, respectively (p = 0.151), in 50% and 68% of patients in groups A1 and B1, respectively (p = 0.620), in 40% and 100% of patients in groups A2 and B2, respectively (p = 0.250), and in 75% and 63% of patients in groups A3 and B3, respectively (p = 0.463). Complications were observed in 13.6% of patients.

Conclusions: Best results were obtained in patients treated with 50 and 100 µg of rt-PA and in those cases BCVA development was more beneficial if additional gas was injected.

PMID: 21332673 [PubMed - as supplied by publisher]

Genetics

Am J Ophthalmol. 2011 Mar;151(3):561-2.

Familial risks of age-related macular degeneration.

Hemminki K, Försti A, Li X, Sundquist K, Sundquist J.

Heidelberg, Germany, and Malmö, Sweden.

PMID: 21335117 [PubMed - in process]

Hum Mol Genet. 2011 Feb 24. [Epub ahead of print]

A CTRP5 Gene S163R mutation Knock-In Mouse Model for Late-Onset Retinal Degeneration.

Chavali VR, Khan NW, Cuckras CA, Bartsch DU, Jablonski MM, Ayyagari R.

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Abstract

Late-onset retinal macular degeneration (L-ORD) is an autosomal dominant inherited disorder caused by a single missense mutation (S163R) in the CTRP5/C1QTNF5 protein. Early phenotypic features of L-ORD include dark adaptation abnormalities, nyctalopia and drusen deposits in the peripheral macular region. Apart from posterior segment abnormalities, these patients also develop abnormally long anterior lens zonules. In the sixth decade of life, the rod and cone function declines, accompanied by electroretinogram (ERG) abnormalities. Some patients also develop choroidal neovascularization (CNV) and glaucoma. In order to understand the disease pathology and mechanisms involved in retinal dystrophy we generated a knock-in (Ctrp5(+/-)) mouse model carrying the disease-associated mutation in the mouse Ctrp5/C1QTNF5 gene. These mice develop slower rod-b wave recovery consistent with early dark adaptation abnormalities, accumulation of hyperautofluorescence spots, retinal pigment epithelium abnormalities, drusen, Bruch's membrane abnormalities, loss of photoreceptors and retinal vascular leakage. The Ctrp5(+/-)mice, which have most of the pathological features of age-related macular degeneration, are unique and may serve as a valuable model both to understand the molecular pathology of late-onset retinal degeneration and to evaluate therapies.

PMID: 21349921 [PubMed - as supplied by publisher]

Epidemiology & pathogenesis

J Coll Physicians Surg Pak. 2011 Feb;21(2):88-92.

Causes of visual impairment in children with low vision.

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Department of Ophthalmology, Hayatabad Medical Complex, Peshawar.

Objective: To determine the main causes of visual impairment in children with low vision. To assess the need of spectacles and low vision devices (LVDs) in children and to evaluate visual outcome after using their LVDs for far and near distance.

Study Design: Observational study. Place and Duration of Study: Khyber Institute of Ophthalmic Medical Sciences, Peshawar, Pakistan, from June 2006 to December 2007.

Methodology: The clinical record of 270 children with low vision age 4-16 years attending the Low Vision Clinic were included. All those children, aged 4-16 years, who had corrected visual acuity (VA) less than 6/18 in the better eye after medical or surgical treatment, were included in the study. WHO low vision criteria were used to classify into visually impaired, severe visually impaired and blind. Results were described as percentage frequencies.

Results: One hundred and eighty nine (70%) were males and 81 (30%) were females. The male to female ratio was 2.3:1. The main causes of visual impairment included nystagmus (15%), Stargardt's disease (14%), maculopathies (13%), myopic macular degeneration (11%) and oculocutaneous albinism (7%). The percentages of visually impaired, severe visually impaired and blind were 33.8%, 27.2% and 39.0% respectively. Spectacles were prescribed to 146 patients and telescopes were prescribed to 75 patients. Spectacles and telescope both were prescribed to 179 patients while Ocutech telescope was prescribed to 4 patients.

Conclusion: Retinal diseases nystagmus and macular conditions were mainly responsible for low vision in children. Visually impaired children especially with hereditary /congenital ocular anomalies benefit from refraction and low vision services which facilitate vision enhancement and inclusive education.

PMID: 21333239 [PubMed - in process]

Ophthalmic Res. 2011 Feb 18;46(3):125-132. [Epub ahead of print]

The Association of Lipoprotein Parameters and C-Reactive Protein in Patients with Age-Related Macular Degeneration.

Colak E, Kosanović-Jaković N, Zorić L, Radosavljević A, Stanković S, Majkić-Singh N.

Institute of Medical Biochemistry, Clinical Center of Serbia and Pharmaceutical Faculty, Clinical Center of Serbia and Medical Faculty, University of Belgrade, Belgrade, Serbia.

Background: Age-related macular degeneration (AMD) is the most common cause of visual impairment in individuals over 50 years of age, with the prevalence of 0.05% before the age of 50 rising to 30% after 74 years of age. An elevated concentration of plasma lipoproteins is considered to be one of the risk factors of AMD development. The aim of our study was to analyze the concentration of serum lipoproteins - total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), non-LDL cholesterol and triglycerides - as well as apolipoproteins - apoA1, apoB and Lp(a) - along with C-reactive protein (CRP) in patients with AMD in order to explore the possible association of lipid and inflammatory parameters with the pathogenesis of AMD.

Material and Methods: In the cross-sectional study in the University clinical setting, 79 patients with AMD, aged 71.47 ± 7.02 years, and 84 aged-matched control subjects were included. The patients underwent

complete ophthalmological examination including visual acuity assessment, color fundus photography and fluorescein angiography.

Results: Statistical processing data revealed significantly higher total (p = 0.0002), LDL (p = 0.023), non-HDL cholesterol (p = 0.0014) and CRP (p = 0.049) values in AMD patients compared to control subjects.

Conclusions: Based on the obtained results, it may be concluded that lipid status disorder and inflammation could play an important role in the development of AMD in elderly people.

PMID: 21336002 [PubMed - as supplied by publisher]

Ophthalmic Res. 2011 Feb 19;46(3):141-144. [Epub ahead of print]

Study of Ethane Level in Exhaled Breath in Patients with Age-Related Macular Degeneration: Preliminary Study.

Cagini C, Giordanelli A, Fiore T, Giardinieri R, Malici B, De Medio GE, Pelli MA, De Bellis F, Capodicasa E.

Departments of Ophthalmology, University of Perugia, Perugia, Italy.

Purpose: A variety of factors have been implicated in the pathogenesis of age-related macular degeneration (ARMD), and oxidative stress plays an important role in the onset and progression of the disease. Breath ethane is now considered a specific and non-invasive test for determining and monitoring the trend of lipid peroxidation and free radical-induced damage in vivo. This test provides an index of the patients' overall oxidative stress level. We evaluated the breath ethane concentration in exhaled air in patients with advanced ARMD.

Methods: In this study, we enrolled 13 patients with advanced ARMD and a control group, and a breath analysis was carried out by gas chromatography.

Results: The mean ethane level in the ARMD patients was 0.82 ± 0.93 nmol/l (range: 0.01-2.7 nmol/l) and the mean ethane value in the control group was 0.12 ± 0.02 nmol/l (range: 0.08-0.16 nmol/l). The difference between the values of the 2 groups was statistically significant (p < 0.005). Receiver operating characteristic analysis showed an elevated area under the curve (0.831; 95% CI: 0.634-0.948), with a significance level of p < 0.0014 (area = 0.5).

Conclusions: These preliminary results seem to indicate that breath ethane levels are higher in most patients with ARMD. The breath ethane test could thus be a useful method for evaluating the level of oxidative stress in patients with ARMD. To our knowledge, there are no data on this type of analysis applied to ARMD.

PMID: 21336004 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2011 Feb;249(2):179-82. Epub 2010 Aug 18.

The rate of myocardial infarction events among patients with age-related macular degeneration: a population-based study.

Golan S, Shalev V, Goldstein M, Treister G, Chodick G, Loewenstein A.

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PURPOSE: To examine the association between age-related macular degeneration (AMD) and the risk of myocardial infarctions (MIs) in a large health maintenance organization.

DESIGN: A retrospective cohort study carried out at Maccabi Healthcare Services (MHS).

PARTICIPANTS: A total of 6,546 patients aged ≥65 years who were diagnosed with AMD between April 18 1996 and June 6 2008, and 61,672 non-AMD patients frequency-matched for age and gender.

METHODS: Participants were retrospectively followed to the day of leaving the MHS, to undergoing an MI, or to closure of the study on July 1 2008, whichever came earlier. The relative risk of MI associated with AMD was estimated using the Cox proportional hazard model.

MAIN OUTCOME MEASURES: Incident myocardial infarction events.

RESULTS: During the study period, there were 159 (5.1 per 1,000 person years [PY]) and 2,997 (4.2 per 1,000 PY) MIs respecively in the AMD and non-AMD patient groups. The age- and gender-adjusted hazard ratio (HR) of MI among AMD patients was 1.01 (95%CI: 0.85-1.20). Baseline medical characteristics associated with increased risk of mortality included diabetes mellitus, hypertension, older age, and male gender. The fully adjusted HR associated with AMD was 1.03 (95%CI: 0.87-1.22).

CONCLUSION: Despite the shared risk factors associated with AMD and MIs, we found no increased risk of MI in AMD patients.

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Kidney function, albuminuria and age-related macular degeneration in NHANES III.

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BACKGROUND: Age-related macular degeneration (AMD) and kidney disease may have shared risk factors, including cardiovascular disease risk factors; additionally AMD and dense deposit disease share a common causal link, with both associated with polymorphisms in the complement pathway. Accordingly, we explored a population-based cohort of US adults to examine if markers of kidney disease identify a higher risk population for prevalent AMD.

METHODS: A cross-sectional nested case-control study matching on age, sex and race was performed using data on adult participants in the Third National Health and Nutrition Examination Survey. Predictor variables included urine albumin-to-creatinine ratio and estimated glomerular filtration rate (eGFR). Study outcomes included late AMD, defined as neovascular disease or geographic atrophy (5:1 matching), and a composite of both early AMD, defined as soft drusen or pigment irregularities with or without any drusen, and late AMD (1:1 matching).

RESULTS: There were 51 participants with late AMD and 865 with any AMD. In conditional logistic regression adjusting for diabetes, hypertension and total cholesterol, lower eGFR was independently associated with late AMD [odds ratio (OR) = 3.05, 95% confidence interval (CI): 1.51-6.13], while albuminuria was not significant. For any AMD, neither albuminuria nor eGFR were significant in adjusted models. In sensitivity analyses excluding diabetics, albuminuria was associated with any AMD (OR = 1.56, 95% CI: 1.11-1.29 and 1.57, 95% CI: 0.61-3.69 for micro- and macroalbuminuria, respectively, P = 0.03).

CONCLUSIONS: Late AMD is more common among individuals with reduced kidney function. Whether this association reflects a common causal pathway or shared risk factors such as hypertension requires additional investigation.

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Macular degeneration: A possible biochemical mechanism.

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Abstract

The possible role of labile endogenous metabolites in the cause of various chronic debilitating diseases such as macular degeneration has not been adequately explored. In the metabolism of the various retinoids, namely retinal (vitamin A aldehyde), retinol (vitamin A alcohol) and retinoic acid, each has the potential for generating labile intermediates, such as their corresponding 5,6-epoxides by the action of various cytochrome P(450)s. Such retinoid epoxides may well have the capacity for acting as toxins upon the neurons in the macula unless they are rapidly hydrolyzed by epoxide hydrolases. Since the cytochrome P(450)s responsible for epoxide formation and the various epoxide hydrolases involved in their hydrolysis are determined genetically, this may serve to explain a genetic component being involved in the causation of age-related macular degeneration.

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OX-LDL Up-Regulates the Vascular Endothelial Growth Factor-to-Pigment Epithelium-Derived Factor Ratio in Human Retinal Pigment Epithelial Cells.

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Purpose: Native and oxidized (OX) low-density lipoprotein (LDL) may contribute to the pathogenesis of age related macular degeneration (AMD). In this study, we investigated the effects of lipoproteins, including LDL and ox-LDL, on cell viability, apoptosis, and vascular endothelial growth factor (VEGF) and pigment epithelium-derived factor (PEDF) expression in cultured human retinal pigment epithelial (RPE) cells.

Method: ARPE-19 cells were incubated with 10-100 mg/ml n-LDL, ox-LDL for 24 hr. Cell viability was assessed using the Cell Titer 96 Aqueous One Solution cell proliferation assay. The apoptosis of RPE was measured with TUNEL. Reverse transcription polymerase chain reaction (RT-PCR) was used to detect the levels of VEGF and PEDF mRNA in RPE cells. The expression of VEGF and PEDF protein was measured by western blotting. To examine the role of MAPK signal transduction in LDL- and OX-LDL-induced VEGF and PEDF protein expression, ARPE-19 cells were pretreated with one of several MAPK inhibitors for 2 hr and then incubated with native LDL or OX-LDL for 24 hr. One-way analysis of variance was used to compare the differences.

Results: OX-LDL treatment decreased ARPE-19 cell viability in a dose-dependent manner, whereas native LDL had no effect. Incubation of ARPE-19 cells with 10 mg/mL OX-LDL induced marked apoptosis, compared with untreated control cells. OX-LDL also increased VEGF expression and decreased PEDF expression, whereas native LDL had no significant effect. The VEGF-to-PEDF ratio was elevated after OX-LDL treatment. OX-LDL-induced VEGF protein synthesis was partly abolished by inhibiting p38 and JNK, while inhibiting ERK did not show a significant effect.

Conclusions: OX-LDL treatment induced cellular changes in ARPE-19 cells that appeared to reflect pathogenic events in neovascular AMD, providing potential insight into the roles of OX-LDL in human RPE cells and its potential role in the pathogenesis of AMD.

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The potential application of iron chelators for the treatment of neurodegenerative diseases.

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Abstract

Many forms of neurodegenerative disease, for instance Alzheimer's disease, Parkinson's disease, Friedreich's ataxia, Hallervorden Spatz syndrome and macular degeneration, are associated with elevated levels of redox active metals in the brain and eye. A logical therapeutic approach therefore, is to remove the toxic levels of these metals, copper and iron in particular, by selective chelation. The increased number of iron-selective chelators now available for clinical use has enhanced interest in this type of therapy. This review summarises the recent developments in the design of chelators for treatment of neurodegenerative disease, identifies some of the essential properties for such molecules and suggests some future strategies.

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