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MD Research News

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Drug treatment

Eye (Lond). 2011 Jan 28. [Epub ahead of print]

Visual perceptions induced by intravitreous injections of therapeutic agents.

Charalampidou S, Nolan J, Ormonde GO, Beatty S.

Institute of Eye Surgery and Institute of Vision Research, Whitfield Clinic, Butlerstown North, Waterford, Ireland.

Purpose: The purpose of this study was to conduct a questionnaire-based survey of subjective visual perceptions induced by intravitreous (IVT) injections of therapeutic agents.

Patients and methods: Patients undergoing an IVT injection of ranibizumab, pegaptanib sodium, or triamcinolone acetonide were administered a questionnaire in the immediate post-injection period and at 2 weeks of follow-up.

Results: In the immediate post-injection period (75 IVT injections, 75 eyes, 75 patients), lights and floaters were reported after 20 (27%) and 24 (32%) IVT injections, respectively. In comparison, at the 2-week follow -up, the incidence of reported lights (11; 15%) was similar (P>0.05), but the incidence of reported floaters was higher (48; 64%; P=0.00). Subgroup analysis for various injection subgroups (no previous injection vs previous injection(s) in the study eye; injections in study eyes with good VA (logarithm of minimal angle of resolution [logMAR] ≤0.3) vs moderate VA (0.7 <logMAR>0.3) vs poor VA (logMAR ≥0.7); injections according to pharmacological agent (ranibizumab vs pegaptanib vs triamcinolone acetonide); injections in study eyes with choroidal neovascularization (of various causes) vs study eyes with macular edema (of various causes); and injections in phakic vs pseudophakic eyes) did not reveal any statistically significant associations. Visual perceptions experienced following 15% of IVT injections gave cause for concern to the patient (mean visual analog scale score (±SD): 4.5 (±1.7)), and in 64% of cases, the patients believed that preoperative counseling would have averted the concern.

Conclusions: Lights and floaters are frequent visual perceptions following IVT injections of therapeutic agents. They can give rise to concern that could be alleviated with preinjection counseling.

Eye advance online publication, 28 January 2011; doi:10.1038/eye.2010.229.

PMID: 21274011 [PubMed - as supplied by publisher]

BMJ. 2011 Jan 6;342:d62. doi: 10.1136/bmj.d62.

Health ministers may call for appraisal of unlicensed cancer drug for eye treatment.

Hawkes N.

PMID: 21212126 [PubMed - indexed for MEDLINE]

Ophthalmologica. 2011 Jan 27;225(3):169-175. [Epub ahead of print]

Photodynamic Therapy Combined with Intravitreal Injection of Vascular Endothelial Growth Factor Antibody for Polypoidal Choroidal Vasculopathy.

Moon SW, Kim MS, Kim ES, Yu SY, Kwak HW.

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Background/Aims: To evaluate the efficacy of photodynamic therapy (PDT) combined with intravitreal injection of anti-vascular-endothelial-growth-factor (anti-VEGF) antibody in patients with polypoidal choroidal vasculopathy (PCV).

Methods: Twenty-two eyes of 22 patients with PCV followed for 12 months after combination therapy with PDT and anti-VEGF were retrospectively reviewed. Patients received intravitreal anti-VEGF (1.25 mg bevacizumab or 0.5 mg ranibizumab) within 7 days after PDT. Retreatment with PDT and intravitreal anti-VEGF injections, or with intravitreal anti-VEGF alone, was performed when indicated. The main outcome measures were best-corrected visual acuity (BCVA) and central foveal thickness (CFT).

Results: Mean logMAR BCVA was 0.43 at baseline and 0.45, 0.36, 0.30 and 0.28 at 1, 3, 6 and 12 months, respectively, after the initial combination therapy. Mean BCVA was significantly improved at 6 and 12 months after treatment ($p < 0.05$). Mean CFT was 269.4 μm at baseline and 180.1, 136.7, 127.5 and 139.6 μm at 1, 3, 6 and 12 months, respectively, after the initial combination therapy. CFT decreased significantly throughout the follow-up period. At 12 months, mean BCVA improved by 1.5 lines, and mean CFT decreased by 129.8 μm. Polypoidal lesions disappeared in 7 of the 13 eyes in which indocyanine green angiography was performed at 12 months. No changes in the branching vascular network were observed in any of these 13 eyes. Patients were treated with PDT a mean of 1.3 times and injected with intravitreal anti-VEGF a mean of 3.4 times over the 12-month period.

Conclusion: Combined PDT and intravitreal anti-VEGF may improve visual acuity and decrease CFT at 12 months. Large long-term prospective studies are needed to evaluate the efficacy and safety of combination therapy.

PMID: 21273795 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Jan 27. [Epub ahead of print]

Inhibition of vascular endothelial growth factor (VEGF) is sufficient to completely restore barrier malfunction induced by growth factors in microvascular retinal endothelial cells.

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Background: Deregulated expression of vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) or insulin-like growth factor-1 (IGF-1) is associated with the pathogenesis of diabetic retinopathy. The VEGF(165)-induced increase in permeability of retinal endothelial cells (REC), probably resulting in diabetic macular oedema (DME), could be completely restored by the VEGF-binding Fab

fragment ranibizumab in vitro. We investigated whether bFGF and IGF-1 as single factors or in combination with VEGF(165) influence permeability and tight junctions in immortalised bovine REC (iBREC) and if these effects could be restored by inhibition of VEGF.

Methods: As a measure of changes in cellular permeability, transendothelial electrical resistance (TER) was monitored during long-term treatment of iBREC with growth factors in the absence or presence of ranibizumab or KRN951 (an inhibitor of VEGF receptors). Expression of claudin-1, as an indicator of functional tight junctions, was assessed by western blot analysis.

Results: Whereas VEGF(165) decreased TER and expression of claudin-1 in a concentration-dependent manner, long-term treatment of iBREC with 10-100 ng/ml bFGF or/and IGF-1 did not. Changes in claudin-1 expression or TER, induced by 25 ng/ml VEGF(165), were slightly enhanced by bFGF and/or IGF-1 and were accompanied by a slightly increased secretion of VEGF. Complete reversion of these effects was achieved by prolonged treatment with ranibizumab and partly by exposure to KRN951.

Conclusion: Our findings indicate that VEGF(165), but not IGF-1 or bFGF, is mainly responsible for changes in cellular permeability observed in REC. This supports VEGF targeting as a therapeutic concept for DME.

PMID: 21273213 [PubMed - as supplied by publisher]

Clin Exp Optom. 2011 Jan 24. doi: 10.1111/j.1444-0938.2010.00570.x. [Epub ahead of print]

Single intravitreal ranibizumab injection in eyes with acute non-arteritic anterior ischaemic optic neuropathy.

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Background: The aim was to evaluate the effect of a single intravitreal ranibizumab injection in eyes with non-arteritic anterior ischaemic optic neuropathy.

Methods: Four eyes of four patients comprised the study group. In addition to a standard ocular examination, visual field testing and retinal nerve fibre layer thickness analysis were performed prior to injection and one and three months after the injection.

Results: Mean time between visual loss and the intravitreal injection was 7.8 days (range, 2-15 days). The mean age of patients was 58.2 years (range, 45-63 years). After a single dose of ranibizumab injection, all patients experienced a visual gain. Mean visual acuity (VA) was 1.15 ± 0.26 logMar before the injection and improved to 0.37 ± 0.09 logMar at the third post-injection month. The mean retinal nerve fibre layer thickness measured with spectral domain optical coherence tomography significantly decreased after the injection in all eyes. No complication related to the injections was observed during the following three months.

Conclusion: Intravitreal ranibizumab injection may be a treatment option in eyes with non-arteritic anterior ischaemic optic neuropathy and a short disease history.

PMID: 21255078 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 Jan 31. [Epub ahead of print]

Genetic association with response to intravitreal ranibizumab (Lucentis(R)) in neovascular AMD patients.

Kloeckener-Gruissem B, Barthelmes D, Labs S, Schindler C, Kurz-Levin M, Michels S, Fleischhauer J, Berger W, Sutter F, Menghini M.

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Purpose: Neovascular age-related macular degeneration (AMD) resulting in decreased central vision severely impairs affected individuals. Current standard treatment is an intravitreal anti-VEGF therapy (ranibizumab), but responses to treatment show large variability. We searched for genetic factors that influence AMD within a Swiss patient population and that affect the outcome of ranibizumab treatment.

Methods: Changes of visual acuity (VA) after initiation of anti-VEGF treatment was followed during 12 months and percentiles of VA course were calculated. Genotypes of polymorphisms in known AMD susceptibility loci (CFH, CFB, HTRA1, AMRS2 and VEGFA) as well as not yet reported AMD associated genes (KDR, LRP5 and FZD4) were determined and their frequencies were compared.

Results: Of the 309 eyes included in the study, 243 completed VA assessment. On average, 3.9 ±2.6 ranibizumab injections were administered. Based on the change of visual acuity, two responder groups were established: 63 eyes were assigned to the poor responders (≤ 25(th) percentile) and 63 eyes to the good responders (≥75(th) percentile). Individuals with genotype CC of p.Y402H in CFH have a decreased chance of positive treatment outcome compared to those with CT and TT genotypes (p=0.005 and p=0.006). In our study genotype combination AG at CFH with CT at FZD4 (SNP rs10898563) promises an increased chance of positive treatment outcome (p=0.004). Furthermore, we confirmed association with the known genetic susceptibility loci CFH, HTRA1 and AMRS2 and identified a risk conferring polymorphism in one new locus, LRP5.

Conclusions: Genetic predisposition may account for the variability in response to anti-VEGF treatment.

PMID: 21282580 [PubMed - as supplied by publisher]

Retina. 2011 Jan 28. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB FOR MACULAR EDEMA SECONDARY TO CENTRAL RETINAL VEIN OCCLUSION.

Risard SM, Pieramici DJ, Rabena MD, Basefsky JC, Avery RL, Castellarin AA, Nasir MA, See RF, Couvillion SS.

From the California Retina Research Foundation, Santa Barbara, California.

PURPOSE: To evaluate the safety and efficacy of intravitreal ranibizumab for macular edema secondary to central retinal vein occlusion.

METHODS: Patients with macular edema secondary to perfused central retinal vein occlusion were enrolled in this ongoing, prospective, open-label study. Treatment was initiated with monthly intravitreal ranibizumab for 3 months. In the first year, additional injections were administered for edema in quarterly intervals as needed (PRN) for Cohort 1 (n = 10) and monthly PRN for Cohort 2 (n = 10). In the second year of treatments, all patients received monthly PRN treatment. Early Treatment Diabetic Retinopathy Study best-corrected visual acuity, central retinal thickness, fundus photographs, and fluorescein angiograms were evaluated, and the incidence and severity of adverse events were documented.

RESULTS: Mean change in best-corrected visual acuity and central retinal thickness improved during the induction phase in both groups. During the remainder of the first year for Cohort 1, initial gains were lost during quarterly treatment but returned with monthly PRN treatment in the second year. For Cohort 2, improvement in best-corrected visual acuity and central retinal thickness from the induction phase was maintained through Month 24. Nineteen of 20 patients experienced a reduction in intraretinal hemorrhage, optic nerve swelling, and/or venous diameter after treatment. One myocardial infarction, one cerebrovascular accident, and no serious ocular adverse events were reported. Iris neovascularization was developed in none of the eyes.

CONCLUSION: Ranibizumab was well tolerated and associated with a greater reduction in macular edema

and improvement in visual acuity in the monthly PRN regimen compared with quarterly treatment. Vision lost during the quarterly PRN injection intervals in the first year of Cohort 1 could be regained by switching to monthly PRN dosing.

PMID: 21283055 [PubMed - as supplied by publisher]

Can J Ophthalmol. 2011 Feb;46(1):46-50.

Management of pediatric choroidal neovascular membranes with intravitreal anti-VEGF agents: a retrospective consecutive case series.

Kohly RP, Muni RH, Kertes PJ, Lam WC.

Objective: To report the results of pediatric choroidal neovascular membranes (CNVMs) secondary to a variety of etiologies treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents.Design: Retrospective case series.

Participants: Four pediatric patients at the Hosptial for Sick Children with CNVMs secondary to a variety of etiologies.

Methods: Each patient received multiple treatments with one of the following anti-VEGF agents: pegaptanib sodium, bevacizumab, or ranibizumab. Progress was monitored by clinical exam, optical coherence tomography (OCT), and fluorescein angiography.

Results: The mean age of our patients was 11.5 years (range, 8-15 years). Patients were followed for a mean of 10 months (range, 4-14 months). One patient was treated with pegaptanib sodium, 2 with bevacizumab, and 1 with ranibizumab. Following treatment, 1 patient showed an improvement and 3 showed stabilization of vision with reduction of fluid on clinical exam and OCT, and cessation of leakage on the fluorescein angiogram. Patients required 2-5 injections of the anti-VEGF agent. No ocular or systemic adverse events were observed in any of our treated patients.

Conclusions: Anti-VEGF agents were effective in the treatment of pediatric CNVMs in this case series. However, we do not know how these results would have differed from other treatment modalities, including observation. We did not observe any adverse side effects; however, larger studies are required to document the safety of these medications in the pediatric population where normal angiogenesis is occurring.

PMID: 21283157 [PubMed - in process]

Open Ophthalmol J. 2010 Oct 21;4:66-9.

Long-term use of intravitreal bevacizumab (avastin) for the treatment of von hippel-lindau associated retinal hemangioblastomas.

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Abstract

Retinal hemangioblastomas are the most common manifestation of Von Hippel-Lindau (VHL) disease [1-3]. While peripheral retinal hemangioblastomas may be treated by thermal laser treatment or cryotherapy, optic nerve and macular lesions are more difficult to treat [4, 5]. Based on the theoretical benefit of administering anti-VEGF treatment, intra-vitreally administered bevacizumab (Avastin, a general pan-VEGF inhibitor) is attractive [6, 7]. Several short-term case series using ranibizumab (Lucentis, mAb fragment of bevacizumab with stronger affinity for VEGF-A) have shown it has promising but minimal success on most

VHL-related hemangioblastomas [8, 9]. A comprehensive study by Wong et al. examined 5 patients over a period up to 61 weeks (47 ± 14 weeks) while Michels et al. examined one patient over a period of 4 months. Due to the short-term nature of these studies, we attempted long-term bevacizumab treatment over 60 months in a monocular subject with progressive visual loss due to a VHL associated macular and optic nerve hemangioblastoma. Over the treatment regimen of 15 injections, visual acuity improved 25 letters, OCT thickness improved from 646 um to 424 um, and structural lesions stabilized while exudates and edema resolved.

PMID: 21293730 [PubMed - in process]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2011 Jan 31. [Epub ahead of print]

Validation of the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) in Age-related Macular Degeneration.

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Purpose: Patient-reported measures of visual function are increasingly incorporated into clinical trials of new treatments for age-related macular degeneration (AMD). Limited information is available regarding the associations between distance visual acuity (VA), reading speed, or contrast sensitivity and the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) subscales judged relevant to these measures. This study's objective was to evaluate such associations along with questions on restricted activity days.

Methods: This cross-sectional study was conducted in patients with a clinical diagnosis of neovascular AMD. Patient-reported outcome measures included the NEI VFQ-25 and restricted activity days. Clinical assessments included best-corrected VA (BCVA), reading speed, and contrast sensitivity. The better-seeing eye was defined based on BCVA of each patient. Psychometric properties of the NEI VFQ-25 were examined; analyses a priori focused on the Near Activities, Distance Activities, and Vision-specific Dependency subscales.

Results: The final study group included 92 participants (mean age, 78 years). Cronbach's alpha for the subscales ranged from 0.67 to 0.92. The NEI VFQ-25 overall composite, Near Activities, Distance Activities, and Vision-specific Dependency scores were correlated with BCVA ($r = -0.48$ to -0.54, all $P<0.0001$), reading speed ($r = 0.43$ to 0.56, all $P<0.0001$), and contrast sensitivity ($r = -0.39$ to -0.46, all $P<0.001$) of the better-seeing eye and with restricted activity days ($r = -0.52$ to -0.55, all $P<0.0001$).

Conclusions: This study provides additional evidence supporting the validity of the NEI VFQ-25 in neovascular AMD patients by demonstrating correlations with a spectrum of vision measurements and a daily function measure.

PMID: 21282568 [PubMed - as supplied by publisher]

IEEE Trans Med Imaging. 2011 Feb;30(2):523-33.

Optimal filter framework for automated, instantaneous detection of lesions in retinal images.

Quellec G, Russell SR, Abramoff MD.

Automated detection of lesions in retinal images is a crucial step towards efficient early detection, or screening, of large at-risk populations. In particular, the detection of microaneurysms, usually the first sign of diabetic retinopathy (DR), and the detection of drusen, the hallmark of age-related macular degeneration

(AMD), are of primary importance. In spite of substantial progress made, detection algorithms still produce 1) false positives-target lesions are mixed up with other normal or abnormal structures in the eye, and 2) false negatives-the large variability in the appearance of the lesions causes a subset of these target lesions to be missed. We propose a general framework for detecting and characterizing target lesions almost instantaneously. This framework relies on a feature space automatically derived from a set of reference image samples representing target lesions, including atypical target lesions, and those eye structures that are similar looking but are not target lesions. The reference image samples are obtained either from an expert- or a data-driven approach. Factor analysis is used to derive the filters generating this feature space from reference samples. Previously unseen image samples are then classified in this feature space. We tested this approach by training it to detect microaneurysms. On a set of images from 2739 patients including 67 with referable DR, DR detection area under the receiver-operating characteristic curve (AUC) was comparable (AUC=0.927) to our previously published red lesion detection algorithm (AUC=0.929). We also tested the approach on the detection of AMD, by training it to differentiate drusen from Stargardt's disease lesions, and achieved an AUC=0.850 on a set of 300 manually detected drusen and 300 manually detected flecks. The entire image processing sequence takes less than a second on a standard PC compared to minutes in our previous approach, allowing instantaneous detection. Free-response receiver-operating characteristic analysis showed the superiority of this approach over a framework where false positives and the atypical lesions are not explicitly modeled. A greater performance was achieved by the expert-driven approach for DR detection, where the designer had sound expert knowledge. However, for both problems, a comparable performance was obtained for both expert- and data-driven approaches. This indicates that annotation of a limited number of lesions suffices for building a detection system for any type of lesion in retinal images, if no expert-knowledge is available. We are studying whether the optimal filter framework also generalizes to the detection of any structure in other domains.

PMID: 21292586 [PubMed - in process]

Ophthalmologica. 2011 Feb 3;225(4):187-192. [Epub ahead of print]

Progress in the Development of Vision Prostheses.

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Abstract

Degenerative retinal diseases like retinitis pigmentosa and age-related macular degeneration are among the most common causes of blindness worldwide. Electronic visual prostheses represent a potential therapeutic option of increasing importance in otherwise incurably impaired patients. Based on extensive animal experiments, several devices are now being tested in clinical trials. According to the placement of the electrodes, possible stimulation sites are located subretinally, epiretinally, along the optic nerve or cortically. Anatomical, physiological and pathophysiological aspects must be considered in development and clinical application. To provide an appropriate retinal substitute, the optimal integration and adaptation of the prosthesis into the highly complex system of the visual pathway is important. This article aims to summarize the relevant studies and provides an overview of the current status of developments and challenges that still need to be mastered.

PMID: 21293161 [PubMed - as supplied by publisher]

Ophthalmologica. 2011 Feb 3;225(4):200-206. [Epub ahead of print]

A Pilot Study on the Combination Treatment of Reduced-Fluence Photodynamic Therapy, Intravitreal Ranibizumab, Intravitreal Dexamethasone and Oral Minocycline for Neovascular Age-Related Macular Degeneration.

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Laser and Retinal Research Unit, King's College Hospital, London, UK.

Aim: To assess the safety and efficacy of the combined treatment of reduced-fluence verteporfin photodynamic therapy (PDT), intravitreal ranibizumab, intravitreal dexamethasone and oral minocycline for choroidal neovascularisa- tion (CNV) secondary to age-related macular degeneration (AMD).

Methods: Nineteen patients with subfoveal CNV secondary to AMD were recruited into the trial. All study eyes (n = 19) received a single cycle of reduced-fluence (25 mJ/cm(2)) PDT with verteporfin followed by an intravitreal injection of ranibizumab 0.3 mg/0.05 ml and dexamethasone 200 µg at baseline. Oral minocycline 100 mg daily was started the following day and continued for 3 months. Patients were followed up monthly for 12 months. Repeat intravitreal ranibizumab was given if best-corrected visual acuity (BCVA) deteriorated by >5 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart or central retinal thickness (CRT) on ocular coherence tomography increased >100 µm.

Results: Eighteen patients completed the 12-month study. Stable vision (loss of ≤15 ETDRS letters) was maintained in 89% eyes (16/18). The mean change in BCVA was -5.0 ± 10.5 ETDRS letters. The mean number of ranibizumab injections was 3.4 (range 2-6). The mean reduction in the CRT was 66.3 µm (±75).

Conclusion: This open-label clinical trial has demonstrated the safety in terms of adverse effects and maintenance of stable vision of combination treatment with verteporfin, ranibizumab, dexamethasone and minocycline in exudative AMD. However, the outcomes with reduced-fluence PDT combination therapy does not differ significantly with outcomes of clinical trials on combination treatment with standard dose PDT and intravitreal ranibizumab in neovascular AMD.

PMID: 21293163 [PubMed - as supplied by publisher]

J Biomed Opt. 2011 January/February;16(1):015001.

New testing software for quantifying discrimination capacity in subjects with ocular pathologies.

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Abstract

We develop a new visual test, designed as software for quantifying discrimination capacity under low-illumination conditions. This is an important task in the presence of visual disturbances, such as those perceived by subjects with some ocular pathologies. For this purpose, we propose a visual-disturbance index, checking the test with two groups of observers having different ocular pathologies: a group with unilateral keratitis and another group affected with age-related macular degeneration (ARMD). To compare the test results to objective data, we use a double-pass device to measure the Strehl ratio, a parameter that quantifies the retinal-image quality, taking into account aberrations, retinal reflection, and intraocular scattering working jointly. Diseased eyes present higher disturbance indexes and a lower Strehl ratio compared to their healthy fellow eyes, registering a significant descending correlation between the disturbance index and the Strehl ratio. The lower the Strehl ratio is, the higher the disturbance index for the eyes studied. Therefore, in keratitis and ARMD eyes, our results demonstrate a deterioration in the retinal-image quality and a lower discrimination capacity to peripheral stimuli, reducing visual performance. The test presented here could be useful for the study and time course in different eye diseases, especially those involving an increase in scattered light or alterations in the ocular media, as shown in this work.

PMID: 21280903 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2011 Jan 29. [Epub ahead of print]

[SPA-2: Semiology for phenotyping AMD: Atrophic AMD.]

[Article in French]

Tahiri Joutei Hassani R, Le Tien V, Canoui-Poitrine F, Atmani K, Querques G, Sterkers M, Massamba N, Coscas G, Soubrane G, Bastuji-Garin S, Souied EH.

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PURPOSE: The determination of homogeneous subgroups of age-related macular degeneration (AMD) is necessary for clinical and genetic studies; therefore, the development of a simple, reproducible, and discriminating classification is essential. In this second part of our study (SPA-2), we evaluated a selected list of items for atrophic AMD based on color photographs of fundus, red-free frames, autofluorescence, fluorescein angiography, indocyanine angiography, and Spectral-Domain OCT.

METHODS: Ten items for atrophy were chosen from the literature and clinical experience. Twenty eyes of 20 patients with atrophic AMD were included. For each patient, the grid was completed by five independent, experienced readers from our reading center and by an expert. The Kappa coefficient was calculated for each item.

RESULTS: The greatest agreement between observers was found for the item "presence of atrophy" (Kappa=1). The worst concordance was recorded for the item "size of atrophy" (Kappa=-0.0286±0.0769 to 0.1813±0.0835).

CONCLUSION: The classification of atrophic AMD is complex and currently not very consensual, hence the need for a discriminant and reproducible classification grid. The evaluation of our grid for atrophic AMD shows satisfactory agreement between observers for the majority of the items. Some modifications are proposed to make it more discriminant and reproducible.

PMID: 21281987 [PubMed - as supplied by publisher]

Epidemiology & pathogenesis

Retina. 2011 Feb 2. [Epub ahead of print]

PREVALENCE OF AGE-RELATED MACULAR DEGENERATION IN RURAL CENTRAL INDIA: The Central India Eye and Medical Study.

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PURPOSE: To evaluate the prevalence of age-related macular degeneration (AMD) in the adult population of rural central India.

METHODS: The population-based Central India Eye and Medical Study was conducted in rural central India and included 4,711 subjects (aged ≥30 years). Age-related macular degeneration was defined by the international classification of the Wisconsin age-related maculopathy grading system.

RESULTS: Fundus photographs were available for 4,542 subjects (96.4%). In subjects aged ≥40, ≥50, and ≥60 years, prevalence of early AMD was 6.1 ± 0.4% (95% confidence interval [CI]: 5.3-6.9%), 8.2 ± 0.6% (95% CI: 7.0-9.4%), and 8.3 ± 0.8% (95% CI: 6.8-9.9%), respectively, and that of late AMD was 0.2 ± 0.8% (95% CI: 0.1-0.4%), 0.2 ± 0.1% (95% CI: 0.1-0.4%), and 0.6 ± 0.2% (95% CI: 0.2-1.0%), respectively. The prevalence of early AMD increased from 1.3 ± 0.3% per subject in the 30-year-old to 40-year-old group, to

3.6 ± 0.5% in the 41-year-old to 50-year-old group, to 7.9 ± 0.9% in the 51-year-old to 60-year-old group, to 10.0 ± 1.1% in the 61-year-old to 70-year-old group, to 8.3 ± 0.2% in the 71-year-old to 80-year-old group, and to 8.0 ± 5.5% in the ≥81-year-old group. Age-related macular degeneration was causative for visual impairment (best-corrected visual acuity in the better eye: <20/60 and ≥20/400) in 3 of 342 subjects (0.9%) and for blindness (visual acuity <20/400) in 0 of 17 subjects.

CONCLUSION: After age adjustment, AMD was found less frequently in the adult population of rural central India than in European populations. Accordingly, visual impairment because of AMD was relatively uncommon in rural central India.

PMID: 21293316 [PubMed - as supplied by publisher]

Ophthalmic Epidemiol. 2011 Feb;18(1):48-52.

Prevalence of age-related macular degeneration in Thailand.

Jenchitr W, Ruamviboonsuk P, Sanmee A, Pokawattana N.

Rangsit University Eye Center and Faculty of Optometry, Rangsit University, Bangkok, Thailand.

Purpose: To determine the prevalence of age-related macular degeneration (AMD) in Thailand.

Methods: In this population-based study, data of participants in the Thailand National Survey of Visual Impairment in 2006-2007 were analyzed. Participants selected for this study were more than 50 years old, and were recruited from 42 districts of 21 provinces. They were interviewed, tested for visual acuity, examined for eye screening, and measured for intraocular pressure. They had digital fundus photographs taken using a nonmydriatic fundus camera through dilated pupils. The diagnosis of AMD, according to the standard international grading system, was made from the interpretation of the digital images by at least 2 retinal specialists. The observed data were used for predicting estimates of the prevalence of AMD in Thailand.

Results: Data from 10,788 participants were analyzed. There were 321/10,788 (3%, 95% CI: 2.7-3.3%) participants diagnosed as having AMD. The mean age was 62.1 (range 50-98, SD 8.8) years old. There were 294 (2.7%) and 27 (0.3%) participants with early AMD (38.4% male) and late AMD (74.1% male) respectively. Of the late AMD, 20 (74.1%) were wet AMD and 7 (25.9%) were geographic atrophy. Based on the population census of Thailand, this could be translated into 351,000 and 39,000 patients with early and late AMD respectively.

Conclusions: Based on these data, it is projected that Thailand will have a large number of late AMD sufferers. This makes it imperative to develop new strategies for the national public health system, aiming to incorporate already available late AMD treatment.

PMID: 21275595 [PubMed - in process]

Pre-clinical

Invest Ophthalmol Vis Sci. 2011 Jan 31. [Epub ahead of print]

Increased neovascularization in mice lacking tissue inhibitor of metalloproteinases-3.

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PURPOSE: Tissue inhibitor of metalloproteinases-3 (TIMP-3) is a matrix bound inhibitor of matrix metalloproteinases (MMPs). The authors have previously determined a novel function of TIMP-3 to inhibit

vascular endothelial growth factor (VEGF)-mediated angiogenesis. Here, the authors examined the in vivo angiogenic phenotype of ocular vessels in mice deficient in TIMP-3.

METHODS: VEGF-mediated corneal neovascularization and laser-induced choroidal neovascularization (CNV) was examined in TIMP-3 null mice. The effects of the absence of TIMP-3 on the phophorylation status of the VEGF-receptor-2 (VEGFR-2) and the downstream signaling pathways were evaluated biochemically. In addition, the activation state of MMPs in the retina of TIMP-3 deficient mice was examined by in situ zymography.

RESULTS: The results of these studies determine an accentuation of pathological VEGF-mediated angiogenesis in the cornea as well as laser-induced CNV in mice lacking TIMP-3. In the absence of the MMP inhibitor, pathophysiological changes are observed in the choroidal vasculature concomitantly with an increase in gelatinolytic activity. These results suggest that an imbalance of extracellular matrix homeostasis together with a loss of an angiogenesis inhibitor can prime vascular beds to be more responsive to an angiogenic stimulus.

CONCLUSIONS: In light of the recent studies, that suggest that genetic variants near TIMP-3 influence susceptibility to age-related macular degeneration, these results imply that TIMP-3 may regulate the development of the choroidal vasculature and is a likely contributor to increased susceptibility to choroidal neovascularization.

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