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Drug treatment

Am J Ophthalmol. 2016 Apr 2. [Epub ahead of print]

Long Term Results of Pro Re Nata Regimen of Aflibercept Treatment in Persistent Neovascular Age-Related Macular Degeneration.

Muftuoglu IK, Arcinue CA, Tsai FF, Alam M, Gaber R, Camacho N, You Q, Freeman WR.

PURPOSE: To determine the 24-month results of patients who had pro-re-nata (PRN) aflibercept treatment due to recurrent or resistant neovascular macular degeneration.

DESIGN: Retrospective, interventional, consecutive case series.

METHODS: Eighty-one eyes of 78 patients with persistent or multiple recurrences of intraretinal or subretinal fluid while receiving monthly bevacizumab or ranibizumab injections and switched to strict, as needed aflibercept treatment with every-8-weeks spectral domain optical coherence tomography (SD-OCT) guided monitoring were included. If there was a persistence of fluid despite this treatment, more frequent aflibercept injections were considered. Anatomic outcomes including maximum retinal thickness, central macular thickness, maximum pigment epithelial detachment height, maximum fluid height and visual acuity (VA) were assessed at given follow-ups.

RESULTS: All anatomic end points significantly improved following 3 consecutive aflibercept injections, which were maintained through 24-months ($p < 0.05$ for all end points at all visits). Thirty-seven eyes (45.6%) required more frequent injections with monthly SD-OCT guided monitoring at a median of 37 weeks (interquartile range, 30-62) to adequately treat the retinal fluid. Seventy-one of 81 eyes (87.7%) became completely dry on at least one follow-up visit, however, there was no significant improvement in VA during the study period.

CONCLUSION: Aflibercept injections with an as needed regimen was effective in many eyes previously treated with monthly bevacizumab or ranibizumab injections that had persistent or recurrent fluid. Despite significant improvement in anatomic outcomes, vision remained stable throughout the 2-year follow-up, likely because this cohort of patients had advanced choroidal neovascular membrane upon enrollment (recurrent or resistant).

PMID: 27049000 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2016 Apr 2. [Epub ahead of print]

Response of pigment epithelial detachment to anti-vascular endothelial growth factor treatment in age-related macular degeneration.

Cho HJ, Kim KM, Kim HS, Lee DW, Kim CG, Kim JW.

OBJECTIVE: To evaluate the therapeutic response of pigment epithelial detachment (PED) to anti-vascular endothelial growth factor (VEGF) treatment in neovascular age-related macular degeneration (nAMD), and identify predictive factors for PED resolution after treatment.

DESIGN: Retrospective, interventional case series.

METHODS: A total of 202 treatment-naïve nAMD eyes presenting PED at baseline were retrospectively included and analyzed. All patients were treated with an initial series of three monthly loading injections of ranibizumab or aflibercept, followed by further injections as required.

RESULTS: After 12 months of treatment, the mean PED height decreased from $453 \pm 261 \mu\text{m}$ at baseline to $230 \pm 142 \mu\text{m}$ ($P=0.002$), and the mean best-corrected visual acuity improved from 0.71 ± 0.41 logarithm of the minimum angle of resolution (Snellen equivalent; 20/102) to 0.60 ± 0.36 (20/79) ($P=0.024$). The proportion of complete PED resolution after treatment was 19.3% (39 eyes). Multivariate logistic regression analysis was used to find baseline characteristics associated with a higher chance of PED resolution, including lower PED height at baseline ($P = 0.018$), polypoidal choroidal vasculopathy ($P = 0.015$) or retinal angiomatous proliferation ($P = 0.010$) compared to typical nAMD, serous PED ($P = 0.022$) compared to fibrovascular PED, and aflibercept ($P = 0.039$) compared to ranibizumab.

CONCLUSIONS: PEDs secondary to nAMD showed significant functional and anatomic improvement after intravitreal anti-VEGF injections over 12 months. However, the anti-VEGF treatment showed limited efficacy for the complete resolution of PED. The PED type, nAMD subtype, baseline PED height, and anti-VEGF drug type was associated with a higher probability of PED resolution after treatment.

PMID: 27048998 [PubMed - as supplied by publisher]

Korean J Ophthalmol. 2016 Apr;30(2):114-20. Epub 2016 Mar 25.

Longitudinal Changes in Retinal Nerve Fiber Layer Thickness after Intravitreal Anti-vascular Endothelial Growth Factor Therapy.

Jo YJ, Kim WJ, Shin IH, Kim JY.

PURPOSE: To determine the effects of intravitreal anti-vascular endothelial growth factor (VEGF) on thickness of the retinal nerve fiber layer (RNFL) in patients with age-related macular degeneration.

METHODS: Twenty eyes of 20 patients diagnosed with age-related macular degeneration who underwent intravitreal anti-VEGF injection were studied. Postinjection RNFL thickness was measured using optical coherence tomography. Average thickness, four-quadrant RNFL thicknesses, and intraocular pressure (IOP) in affected eyes were measured before and 6 and 12 months after anti-VEGF injection for comparison. RNFL thickness and IOP in affected and normal fellow eyes were also compared. Given that macular lesions can affect RNFL thickness, the changes in thickness were evaluated by dividing the 12 clock-hour RNFL into the pathologic areas adjacent to the lesion and the non-pathologic area.

RESULTS: The mean clock-hour segment in the pathologic area was 4.8 hours. A significantly thicker RNFL was exhibited in temporal quadrants and pathologic areas ($p = 0.043$ and 0.048 , respectively) in affected eyes before injection compared to the baseline RNFL thickness in normal eyes. No significant differences were found in RNFL thickness or IOP between affected and normal eyes after injection. The changes over time in the temporal and pathologic areas were statistically significant at 6 and 12 months after injection compared to baseline data ($p < 0.05$). No significant differences were displayed in RNFL thickness in the other three quadrants or in non-pathologic areas in either affected or normal eyes. Sequential changes in RNFL thickness in affected eyes were not significant.

CONCLUSIONS: Repeat intravitreal anti-VEGF treatment did not have a significant effect on RNFL thickness. RNFL thickness significantly decreased with time in the pathologic areas and in the temporal segment adjacent to exudative macular lesions. The reduction in RNFL thickness was most likely associated with changes in the macular lesion rather than with anti-VEGF injection.

PMID: 27051259 [PubMed - in process] PMCID: PMC4820521

Ophthalmic Res. 2016 Apr 6;56(1). [Epub ahead of print]

Long-Term Effect of Anti-VEGF Agents on Intraocular Pressure in Age-Related Macular Degeneration.

Beato J, Pedrosa AC, Pinheiro-Costa J, Freitas-da-Costa P, Falcão MS, Melo A, Estrela-Silva S, Falcão-Reis F, Carneiro ÂM.

PURPOSE: To analyze the effect of anti-vascular endothelial growth factor (VEGF) agents on intraocular pressure (IOP) in patients with neovascular age-related macular degeneration (AMD). **Materials and Methods:** This is a retrospective study that included 72 patients treated unilaterally with anti-VEGF agents according to a pro re nata regimen. Fellow noninjected eyes (n = 72) were used as controls. IOP variation and the development of sustained ocular hypertension (OHT) were assessed both in the injected and in the fellow eyes.

RESULTS: While the final IOP was not significantly different between the 2 groups, sustained OHT developed in 4.2% of the injected eyes and 1.4% of the controls. In the study group, no significant IOP variation was noted during follow-up in patients receiving ≤ 20 injections, but there was a significant increase in IOP with time in more frequently treated patients ($p = 0.041$). Comparison of both subgroups demonstrated that patients receiving >20 injections suffered significantly greater IOP variation ($p = 0.034$) during follow-up, and that these patients tended to require IOP-lowering treatment more frequently ($p = 0.090$).

CONCLUSION: Multiple anti-VEGF injections lead to an increase in IOP, although this variation is not sufficient to cause development of OHT in the majority of patients.

PMID: 27046391 [PubMed - as supplied by publisher]

J Ophthalmol. 2016;2016:4095852. Epub 2016 Mar 6.

A Meta-Analysis of Studies Evaluating Visual and Anatomical Outcomes in Patients with Treatment Resistant Neovascular Age-Related Macular Degeneration following Switching to Treatment with Aflibercept.

Seguin-Greenstein S, Lightman S, Tomkins-Netzer O.

Abstract: With the introduction of aflibercept, eyes with neovascular age-related macular degeneration (AMD) not responding well to injections of ranibizumab or bevacizumab can be switched to treatment with aflibercept. We carried out a meta-analysis to analyze all available evidence of visual and anatomical outcomes of eyes with resistant neovascular AMD switched to aflibercept at six months. Data from seven retrospective and prospective studies looking at change in best corrected visual acuity (BCVA) and central retinal thickness (CRT) were included. Weighted mean difference (WMD) and 95% CI were estimated using the standardized mean change method. The overall results of the meta-analysis showed a small but statistically significant improvement in BCVA six months following treatment switch to aflibercept (WMD 0.142, 95% CI 0.006 to 0.28; $p = 0.04$), and the effect was more significant in data gathered from prospective studies (WMD 0.407, 95% CI 0.023 to 0.791, $p = 0.038$). There was a significant improvement in CRT following treatment switch to aflibercept (WMD -0.36, 95% CI -0.485 to -0.235; $p < 0.0001$). Our meta-analysis indicates that following treatment switch to aflibercept patients may have a significant improvement in CRT with stabilization or even some improvement in their visual acuity.

PMID: 27042342 [PubMed] PMCID: PMC4799814

Surv Ophthalmol. 2016 Apr 1. [Epub ahead of print]

Vascular Endothelial Growth Factor and Diabetic Macular Edema.

Lally DR, Shah CP, Heier JS.

Abstract: Diabetes mellitus is a major global health epidemic, and diabetic macular edema (DME) is the leading cause of vision loss in this population. Macular focal and/or grid laser photocoagulation applied to microaneurysms and thickened retina had long been primary therapy for DME. Chronically elevated serum glucose is known to cause breakdown in the inner and outer retinal blood barrier resulting in up-regulation of vascular endothelial growth factor (VEGF). Intravitreal anti-VEGF agents, including ranibizumab, bevacizumab, and aflibercept, have been shown in randomized clinical trials to be superior to macular laser for the treatment of clinically relevant DME. The READ-2, RISE/RIDE, and RESTORE trials established ranibizumab's superiority to macular laser, while the BOLT trial demonstrated bevacizumab's superiority to laser. The DRCR.net Protocol T results showed that intravitreal aflibercept, bevacizumab and ranibizumab were all effective in reducing retinal thickness secondary to diabetic edema and in improving vision due to this cause. When the presenting vision was 20/40 or better, visual improvement was equivalent. With eyes presenting with 20/50 or worse vision, aflibercept was superior with respect to visual improvement. Intravitreal anti-VEGF therapy can be burdensome for the patient and healthcare system, often requiring monthly treatment visits. In order to reduce burdens, anti-VEGF strategies are in development to lengthen the treatment interval.

PMID: 27045225 [PubMed - as supplied by publisher]

Int Ophthalmol. 2016 Apr 4. [Epub ahead of print]

Outcome of intravitreal dexamethasone implant for the treatment of ranibizumab-resistant macular edema secondary to retinal vein occlusion.

Manousaridis K, Peter S, Mennel S.

Abstract: To assess the effect of intravitreal dexamethasone implant (Ozurdex) for the treatment of macular edema secondary to retinal vein occlusion (RVO) resistant to repeated intravitreal ranibizumab injection. Retrospective review of 11 patients (11 eyes) with ranibizumab-resistant macular edema secondary to RVO. Macular edema was considered refractory to ranibizumab if no change of the pattern of macular fluid on optical coherence tomography and no change of best-corrected visual acuity (BCVA) was observed after at least three consecutive monthly injections, excluding the loading dose. A single Ozurdex injection was performed and BCVA and central foveal thickness (CFT) were reviewed 2, 3, and 6 months after treatment. Mean BCVA improved significantly from 0.51 logarithm of the minimal angle of resolution (log MAR) at baseline to 0.3 log MAR ($p = 0.03$) at 2 months and 0.29 log MAR ($p = 0.003$) at 3 months. There was no significant difference in the BCVA between baseline at 6 months ($p = 0.62$). Mean CFT reduced significantly from 538 μm at baseline to 281 μm at 2 months ($p = 0.00003$), 281 μm at 3 months ($p = 0.00003$), and 445 μm at 6 months ($p = 0.03$). Treatment with Ozurdex results in improvement of BCVA and reduction of CFT in patients with ranibizumab refractory macular edema due to RVO at 3 months. However, it seems that the visual acuity gain may not last up to 6 months, so that a re-injection before this time point could be considered.

PMID: 27043320 [PubMed - as supplied by publisher]

BMC Ophthalmol. 2016 Apr 5;16(1):36.

Correlation between optic nerve head circulation and visual function before and after anti-VEGF therapy for central retinal vein occlusion: prospective, interventional case series.

Nagasato D, Mitamura Y, Semba K, Akaiwa K, Nagasawa T, Yoshizumi Y, Tabuchi H, Kiuchi Y.

BACKGROUND: To determine the correlation between the optic nerve head (ONH) circulation determined by laser speckle flowgraphy and the best-corrected visual acuity or retinal sensitivity before and after intravitreal bevacizumab or ranibizumab for central retinal vein occlusion.

METHODS: Thirty-one eyes of 31 patients were treated with intravitreal bevacizumab or ranibizumab for

macular edema due to a central retinal vein occlusion. The blood flow in the large vessels on the ONH, the best-corrected visual acuity, and retinal sensitivity were measured at the baseline, and at 1, 3, and 6 months after treatment. The arteriovenous passage time on fluorescein angiography was determined. The venous tortuosity index was calculated on color fundus photograph by dividing the length of the tortuous retinal vein by the chord length of the same segment. The blood flow was represented by the mean blur rate (MBR) determined by laser speckle flowgraphy. To exclude the influence of systemic circulation and blood flow in the ONH tissue, the corrected MBR was calculated as MBR of ONH vessel area - MBR of ONH tissue area in the affected eye divided by the vascular MBR - tissue MBR in the unaffected eye. Pearson's correlation tests were used to determine the significance of correlations between the MBR and the best-corrected visual acuity, retinal sensitivity, arteriovenous passage time, or venous tortuosity index.

RESULTS: At the baseline, the corrected MBR was significantly correlated with the arteriovenous passage time and venous tortuosity index ($r = -0.807$, $P < 0.001$; $r = -0.716$, $P < 0.001$; respectively). The corrected MBR was significantly correlated with the best-corrected visual acuity and retinal sensitivity at the baseline, and at 1, 3, and 6 months (all $P < 0.050$). The corrected MBR at the baseline was significantly correlated with the best-corrected visual acuity at 6 months ($r = -0.651$, $P < 0.001$) and retinal sensitivity at 6 months ($r = 0.485$, $P = 0.005$).

CONCLUSIONS: The pre-treatment blood flow velocity of ONH can be used as a predictive factor for the best-corrected visual acuity and retinal sensitivity after anti-VEGF therapy for central retinal vein occlusion.

PMID: 27044276 [PubMed - in process] PMCID: PMC4820868

Ophthalmology. 2016 Mar 30. [Epub ahead of print]

Individualized Stabilization Criteria-Driven Ranibizumab versus Laser in Branch Retinal Vein Occlusion: Six-Month Results of BRIGHTER.

Tadayoni R, Waldstein SM, Boscia F, Gerding H, Pearce I, Priglinger S, Wenzel A, Barnes E, Gekkieva M, Pilz S, Monés J; BRIGHTER study group.

PURPOSE: To compare the 6-month efficacy and safety profile of an individualized stabilization criteria-driven pro re nata (PRN) regimen of ranibizumab 0.5 mg with or without laser versus laser alone in patients with visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO).

DESIGN: A 24-month, prospective, open-label, randomized, active-controlled, multicenter, phase IIIb study.

PARTICIPANTS: A total of 455 patients.

METHODS: Eligible patients were randomized 2:2:1 to receive ranibizumab ($n = 183$), ranibizumab with laser ($n = 180$), or laser only ($n = 92$). Patients treated with ranibizumab with or without laser received a minimum of 3 initial monthly ranibizumab injections until visual acuity (VA) stabilization, and VA-based PRN dosing thereafter. In the ranibizumab with laser and laser-only groups, laser was given at the investigator's discretion at a minimum interval of 4 months and if VA was <79 letters.

MAIN OUTCOME MEASURES: Mean change from baseline at month 6 in best-corrected visual acuity (BCVA) (primary end point) and central subfield thickness, and safety over 6 months. Exploratory objectives were to evaluate the influence of baseline BCVA, disease duration, and ischemia on BCVA outcomes at month 6.

RESULTS: Baseline mean BCVA was 57.7 letters, and mean BRVO duration was 9.9 months. Ranibizumab with or without laser was superior to laser only in improving mean BCVA from baseline at month 6 (14.8 and 14.8 vs. 6.0 letters; both $P < 0.0001$; primary end point met). Patients with a shorter BRVO duration at baseline had a higher mean BCVA gain than those with a longer BRVO duration. Patients with a poor baseline VA had a better BCVA gain than those with a higher baseline VA, although final BCVA was lower in those with poor baseline VA. In the ranibizumab with or without laser groups, the presence of some macular ischemia at baseline did not influence mean BCVA gains. There were no new

ocular or nonocular safety events.

CONCLUSIONS: Ranibizumab with an individualized VA-based regimen, with or without laser, showed statistically significant superior improvement in BCVA compared with laser alone in patients with BRVO. Overall, there were no new safety events other than those reported in previous studies.

PMID: 27039022 [PubMed - as supplied by publisher] Free full text

Eye (Lond). 2016 Apr 8. [Epub ahead of print]

Vitrectomy with subretinal tissue plasminogen activator and ranibizumab for submacular haemorrhages secondary to age-related macular degeneration: retrospective case series of 45 consecutive cases.

González-López JJ, McGowan G, Chapman E, Yorston D.

Purpose: To assess the efficacy of small-gauge vitrectomy with subretinal recombinant tissue plasminogen activator (rtPA) and ranibizumab for submacular haemorrhages secondary to neovascular age-related macular degeneration (nAMD), and to identify the factors associated with visual outcome.

Methods: A retrospective case series was performed, including all patients who had small-gauge vitrectomy with subretinal rtPA and ranibizumab for submacular haemorrhages secondary to nAMD. All patients received three consecutive monthly injections of ranibizumab after the surgery, and were reviewed monthly and treated on a pro re nata regime.

Results: A total of 45 eyes of 45 patients were included in the study. Mean age was 77.07 ± 9.67 years, and 32 of 45 patients (71.1%) were women. Surgery was performed on average 6.98 ± 5.70 days after the onset of symptoms, and patients were observed for a follow-up period of 12.9 ± 10.8 months. On average, visual acuity improved -0.59 ± 0.61 LogMAR between presentation and last follow-up. Visual acuity improved in 33 patients (73.3%), remained unchanged in 10 patients (22.2%), and worsened in 2 patients (4.4%). Multiple linear regression showed that patients with smaller haemorrhages ($P=0.012$) and prompt surgery ($P=0.008$) had better final visual acuities. A haemorrhage area of ≤ 30 mm² had 91.3% sensitivity and 73.3% specificity for predicting a final visual acuity $\geq 6/60$.

Conclusion: Small-gauge vitrectomy with subretinal rtPA and ranibizumab is effective for improving visual acuity in patients with submacular haemorrhages secondary to nAMD. Small haemorrhage area and prompt surgery are associated with better final visual acuity.

PMID: 27055681 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Ophthalmology. 2016 Mar 31. [Epub ahead of print]

Pseudodrusen and Incidence of Late Age-Related Macular Degeneration in Fellow Eyes in the Comparison of Age-Related Macular Degeneration Treatments Trials.

Zhou Q, Daniel E, Maguire MG, Grunwald JE, Martin ER, Martin DF, Ying GS.

PURPOSE: To evaluate the association between pseudodrusen and incidence of late age-related macular degeneration (AMD) in fellow eyes of patients with unilateral neovascular AMD (nAMD).

DESIGN: Cohort study within the Comparison of AMD Treatments Trials (CATT).

PARTICIPANTS: Patients with neither nAMD nor geographic atrophy (GA) in the fellow eye at baseline.

METHODS: Presence and type (dot, reticular, or confluent) of baseline pseudodrusen were assessed using

digital color fundus photography (CFP) viewed under full color, green channel, and blue channel; red-free images; and fluorescein angiography (FA). Incidence of nAMD was based on monthly clinical examination and reading center evaluation of images at years 1 and 2. Incidence of GA was based on reading center evaluation of CFP and FA images at years 1 and 2. Associations of baseline pseudodrusen with incident nAMD and GA were summarized with adjusted risk ratios (aRRs) and their 95% confidence intervals (CIs) from multivariate Cox models, with adjustment of covariates identified through backward stepwise selection.

MAIN OUTCOME MEASURES: Incident nAMD and GA.

RESULTS: Among 620 fellow eyes, 176 (28.4%) had baseline pseudodrusen (55% dot, 82% reticular, 35% confluent). Within 2 years, nAMD occurred in 54 eyes (30.7%) with pseudodrusen and in 72 eyes (16.2%) without pseudodrusen (aRR, 2.05; 95% CI, 1.43-2.93); GA occurred in 27 eyes (15.3%) with pseudodrusen and in 37 eyes (8.3%) without pseudodrusen (aRR, 1.89; 95% CI, 1.13-3.17); late AMD occurred in 73 eyes (41.5%) with pseudodrusen and in 101 eyes (22.8%) without pseudodrusen (aRR, 2.07; 95% CI, 1.51-2.83). Dot pseudodrusen were associated independently with nAMD (aRR, 2.53; 95% CI, 1.60-4.00), whereas confluent pseudodrusen were associated independently with GA (aRR, 4.35; 95% CI, 1.69-11.2). Eyes with pseudodrusen had increased incidence of late AMD regardless of whether the Age-Related Eye Diseases Study (AREDS) severity score was 2 (28.7% vs. 10.3%), 3 (34.9% vs. 13.7%), or 4 (50.5% vs. 32.0%).

CONCLUSIONS: In fellow eyes of CATT participants, pseudodrusen were associated independently with a higher incidence of both nAMD and GA. Dot pseudodrusen were associated with nAMD, whereas confluent pseudodrusen were associated with GA. Pseudodrusen should be considered along with the AREDS severity score for predicting late AMD.

PMID: 27040149 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2016 Apr 4. [Epub ahead of print]

Drusen volume development over time and its relevance to the course of age-related macular degeneration.

Schlanitz FG, Baumann B, Kundi M, Sacu S, Baratsits M, Scheschy U, Shahlaee A, Mittermüller TJ, Montuoro A, Roberts P, Pircher M, Hitzenberger CK, Schmidt-Erfurth U.

AIMS: To quantify the change in drusen volume over time and identify its prognostic value for individual risk assessment.

METHODS: A prospective observational study over a minimum of 3 years and maximum of 5 years and follow-up examination every 3 months was conducted at the ophthalmology department of the Medical University of Vienna. 109 patients presenting early and intermediate age-related macular degeneration (AMD) were included, of which 30 patients concluded a regular follow-up for at least 3 years. 50 eyes of 30 patients were imaged every 3 months using spectral-domain and polarisation-sensitive optical coherence tomography (OCT). Drusen volume was measured using an automated algorithm. Data of a 6-month follow-up were segmented manually by expert graders.

RESULTS: Gradings from 24 000 individual B-scans showed solid correlation between manual and automated segmentation with an initial mean drusen volume of 0.17 mm³. The increase in drusen volume was shown to be comparable among all eyes, and a model for long-term drusen volume development could be fitted as a cubic polynomial function and an R²=0.955. Spontaneous drusen regression was observed in 22 of 50 eyes. In this group, four eyes developed choroidal neovascularisation and three geographic atrophy.

CONCLUSIONS: Drusen volume increase over time can be described by a cubic function. Spontaneous regression appears to precede conversion to advanced AMD. OCT might be a promising tool for predicting the individual risk of progression of AMD.

PMID: 27044341 [PubMed - as supplied by publisher]

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Medicine (Baltimore). 2016 Apr;95(14):e3264.

Optical Coherence Tomography Angiography Of Pathological Myopia Sourced and Idiopathic Choroidal Neovascularization With Follow-Up.

Liu B, Bao L, Zhang J.

Abstract: To observe optical coherence tomography angiography (OCTA) images during follow-up of choroidal neovascularization (CNV) caused by pathological myopia (PM) or idiopathy and discuss OCTA's clinical applications. Patients with CNV caused by PM or idiopathic CNV (ICNV) were recruited prospectively from the Department of Ophthalmology, West China Hospital from March 2015 to June 2015. Intravitreal injections of Ranibizumab were conducted on all patients and repeated treatments were performed based on examinations of follow-up. Patients received OCTA the first week after injection, together with measurements of best-corrected visual acuity (BCVA) and central macular thickness (CMT). Subsequent follow-up was done once a month. About 10 eyes of 10 patients were included in this study and mean age was (46.20 ± 10.15) years old. Around 6 (60%) were females and the other 4 (40%) were males and 5 were diagnosed with PM and 5 were ICNV. Mean follow-up was (7.82 ± 2.47) weeks. Except 4 (40%) patients got only 1 injection, 5 (50%) received two injections, and 1 (10%) patient got 4 (once every two weeks) due to his treatment-resistant lesion. Endpoint date of this study was on 25th June, 2015. Mean baseline BCVA was (0.81 ± 0.45) logarithm of minimal angle resolution (logMAR) and increased significantly to (0.50 ± 0.40) at last follow-up ($P=0.005$). Average CMT of baseline was (276.90 ± 69.73) μ m and decreased to (249.70 ± 53.37) μ m at final follow-up with the statistical significance ($P=0.008$). OCTA demonstrated details of reduction of CNV size and vessel density simultaneously. OCTA could demonstrate the valid CNV form having advantages of rapid, noninvasive and repeatable. Combination of OCTA and other examinations had a promising future of clinical application on ocular neovascularization diseases. Further studies with larger sample size and longer follow-up are necessary and more advanced OCTA is being expected.

PMID: 27057880 [PubMed - in process]

Clin Ophthalmol. 2016 Mar 11;10:431-6. eCollection 2016.

Three-year results of a modified photodynamic therapy procedure (Ironing PDT) for age-related macular degeneration patients with large lesions.

Otsuji T, Sho K, Tsumura A, Koike N, Nishimura T, Takahashi K.

BACKGROUND: To evaluate the effect of photodynamic therapy (PDT) using a modified procedure on exudative age-related macular degeneration having been conventionally difficult to treat.

METHODS: The medical records of eight consecutive patients (eight eyes) with age-related macular degeneration treated with modified PDT were reviewed retrospectively. Modified PDT was used for the lesions that could not be covered by conventional use of PDT, either because the lesion was too large or too close to the optic disc. A moving PDT laser spot at constant speed, for 83 seconds, was used to cover the entire lesion, and was named "Ironing PDT." This retrospective study was performed with informed patient consent. It was approved by the Institutional Review Board of Kansai Medical University.

RESULTS: No exudation could be found 36 months after treatment in five eyes (62.5%). There was no significant difference between the best-corrected visual acuity before PDT (0.95 logMAR) and after PDT (1.09 logMAR). The logMAR best-corrected visual acuity was improved in one eye, maintained in five eyes, and deteriorated in two eyes.

CONCLUSION: Ironing PDT decreased subfoveal fluid and preserved visual acuity in some patients with age-related macular degeneration difficult to treat with conventional therapy.

PMID: 27041985 [PubMed] PMCID: PMC4795568

Arch Soc Esp Oftalmol. 2016 Mar 30. [Epub ahead of print]

Bilateral polypoidal choroidal vasculopathy coexisting with exudative and atrophic age-related macular degeneration. [Article in English, Spanish]

Aronés-Santivañez JR, Dyrda A, Alarcón Valero I.

OBJECTIVE: To present the case of simultaneous presentation of polypoidal choroidal vasculopathy (PCV) and aged-related macular degeneration (AMD).

CASE REPORT: An 83-year-old woman presented with decreased vision in the left eye (LE). In the examination there was an orange peripapillary lesion surrounded by lipid exudates and another subfoveal greyish lesion in the LE. Disciform scarring was observed in the right eye. Fluorescein angiography showed a classic neovascular membrane in in the LE fovea. Indocyanine angiography (ICGA) showed a polyp-like peri-papillary aneurysmal dilation in both eyes. The patient was treated with photodynamic therapy and anti-VEGF injections with stabilisation of the lesions.

CONCLUSION: PCV and AMD can co-exist in unusual cases. When PCV is suspected, ICGA is mandatory for diagnosis.

PMID: 27038540 [PubMed - as supplied by publisher]

Pathogenesis

Ophthalmic Res. 2016 Apr 9;56(1). [Epub ahead of print]

Inhibitory Effect of Chrysin (5,7-Dihydroxyflavone) on Experimental Choroidal Neovascularization in Rats.

Song JH, Kim YH, Lee SC, Kim MH, Lee JH.

PURPOSE: The aim of this study was to evaluate the effect of chrysin on laser-induced experimental choroidal neovascularization (CNV) in a rat model.

METHODS: Male brown Norway rats were anesthetized, and a diode laser was used to break Bruch's membrane. One week later, each rat was intravitreally injected with 5 µl of 15 mg/ml chrysin, and CNV development was determined by fluorescein angiography at 2 weeks. The effect of chrysin on experimental CNV was assessed by fluorescein angiography and histology.

RESULTS: Two weeks after laser treatment, the intensity of fluorescein leakage from the photocoagulated lesions decreased significantly compared with the control group ($p = 0.044$). When the lesions were categorized into low- and high-leakage groups, there was a significant correlation between chrysin treatment and degree of leakage ($p = 0.028$). Compared with the chrysin-treated group, the relative risk of developing high-leakage lesions in the control group was 3.18. The mean CNV thickness was significantly thinner in chrysin-treated eyes than in control eyes (34.13 ± 0.88 vs. 37.76 ± 0.90 µm, $p = 0.005$).

CONCLUSION: Chrysin has an inhibitory effect on CNV in an experimental rat model, indicating that chrysin should be further evaluated for its potential as a therapy for CNV in age-related macular degeneration and in other vision-threatening conditions associated with CNV.

PMID: 27058958 [PubMed - as supplied by publisher]

Assay Drug Dev Technol. 2016 Apr 5. [Epub ahead of print]

Closantel Suppresses Angiogenesis and Cancer Growth in Zebrafish Models.

Zhu XY, Xia B, Liu HC, Xu YQ, Huang CJ, Gao JM, Dong QX, Li CQ.

Abstract: Angiogenesis has emerged as an important therapeutic target in several major diseases, including cancer and age-related macular degeneration. The zebrafish offer the potential for high-throughput drug discovery in a whole vertebrate system. In this study, we have taken advantage of the transgenic Tg (fli1a:EGFP) zebrafish line to screen the U.S. Drug Collection Library and identified 11 old drugs with antiangiogenic activity, including Closantel, an FDA-approved broad-spectrum salicylanilide antiparasitic drug for a variety of types of animals. Closantel was confirmed to have antiangiogenic activity in zebrafish with a half-inhibitory concentration (IC₅₀) at 1.69 μ M on the intersegmental vessels and 1.45 μ M on the subintestinal vessels. Closantel also markedly suppressed cancer growth in zebrafish xenotransplanted with human lymphoma, cervical cancer, pancreatic cancer, and liver cancer cells, generally in a dose-dependent manner. These data reveal that Closantel has antiangiogenesis and anticancer effects and could be a potential drug candidate for animal and human cancer treatments. Further study is needed to clarify the mechanisms involved in the antiangiogenesis and anticancer effects of Closantel.

PMID: 27045536 [PubMed - as supplied by publisher]

PLoS One. 2016 Apr 5;11(4):e0153292.

Correction: microRNA-34a-Mediated Down-Regulation of the Microglial-Enriched Triggering Receptor and Phagocytosis-Sensor TREM2 in Age-Related Macular Degeneration.

PLOS ONE Staff.

Abstract

[This corrects the article DOI: 10.1371/journal.pone.0150211.].

Erratum for

microRNA-34a-Mediated Down-Regulation of the Microglial-Enriched Triggering Receptor and Phagocytosis-Sensor TREM2 in Age-Related Macular Degeneration. [PLoS One. 2016]

PMID: 27045660 [PubMed - as supplied by publisher]

Epidemiology

JAMA Ophthalmol. 2016 Apr 7. [Epub ahead of print]

Prevalence of Age-Related Macular Degeneration in Chinese American Adults: The Chinese American Eye Study.

Varma R, Choudhury F, Chen S, Wu S, Hsu C, Torres M, Klein R, Azen SP, McKean-Cowdin R; Chinese American Eye Study Group.

IMPORTANCE: Population-based prevalence estimates of age-related macular degeneration (AMD) need to be determined to assess its burden among Chinese Americans, the fastest growing racial group in the United States.

OBJECTIVE: To determine the age- and sex- specific prevalence of AMD among Chinese Americans.

DESIGN: The Chinese American Eye Study (CHES) was conducted in a general urban community of 10 census tracts in Monterey Park, California. A total of 4582 Chinese American adults aged 50 years or older participated in this population-based, cross-sectional study from February 16, 2010, through October 9, 2013, and underwent an interview as well as comprehensive clinical and eye examinations, including detailed retinal photography of both eyes. Fundus photographs were graded for drusen and retinal pigment epithelium abnormalities and were evaluated for AMD.

MAIN OUTCOMES AND MEASURES: The prevalence of early and advanced AMD, drusen, geographic atrophy, and neovascular AMD were determined by using a modified Wisconsin Age-Related Maculopathy Grading Scale (a 6-level scale: 10, no AMD; 60, advanced AMD).

RESULTS: Of the 4582 participants completing both the home survey and clinical examination, 4172 individuals (91.1%) had at least 1 gradable photograph. A total of 1526 (36.6%) participants were men, and the mean (SD) age was 61.2 (8.8) years. When examined by 10-year age groups, the prevalence of early AMD ranged from 5.8% (n = 119) in participants aged 50 to 59 years to 17.6% (n = 37) in those 80 years or older, retinal pigment epithelium abnormalities from 4.1% (n = 85) to 7.2% (n = 16), large drusen ($\geq 125 \mu\text{m}$) from 9.8% to 32.4%, soft drusen from 27.6% (n = 567) to 58.6% (n = 123), and soft indistinct drusen from 3.7% (n = 76) to 15.2% (n = 32). The prevalence of advanced AMD ranged from 0.2% (n = 3) in participants aged 50 to 59 years to 1.0% (n = 2) in those 80 years or older. Of the 14 cases of advanced AMD, 85.7% (95% CI, 57.2%-98.2%; n = 12) were neovascular AMD and 14.3% (95% CI, 2.0%-42.8%; n = 2) were geographic atrophy. Acute macular degeneration was more common in men (10.9% [9.3%-12.5%]; n = 166) than women (5.8% [4.9%-6.7%]; n = 154) in this cohort.

CONCLUSIONS AND RELEVANCE: Data from CHES suggest that Chinese Americans have a lower prevalence of early and advanced AMD compared with non-Hispanic white individuals. The prevalence of early AMD, advanced AMD, and large drusen was higher among Chinese Americans in CHES than among the Chinese population living in urban/rural China but lower than that in urban-dwelling Taiwanese.

PMID: 27055183 [PubMed - as supplied by publisher]

Biomed Res Int. 2016;2016:6215745. Epub 2016 Mar 14.

Eclectic Ocular Comorbidities and Systemic Diseases with Eye Involvement: A Review.

Pinazo-Durán MD, Zanón-Moreno V, García-Medina JJ, Arévalo JF, Gallego-Pinazo R, Nucci C.

Abstract: Coexistence of several ocular diseases is more frequent than suspected. In spite of the refractive errors, one or more of the following can be detected simultaneously: glaucoma, cataracts, uveitis, age-related macular degeneration, and dry eyes. In addition, as people age, ocular comorbidities are much more usually seen. Specific diseases are openly acknowledged to affect the eyes and vision, such as diabetes mellitus, hypertension blood pressure, arthritis, hyperthyroidism, neurodegenerative disorders, hematologic malignancies, and/or systemic infections. Recent advances in early diagnosis and therapy of the ophthalmic pathologies have reinforced patient options to prevent visual impairment and blindness. Because of this, it is essential not to overlook sight-threatening conditions such as the ocular comorbidities and/or the eye involvement in the context of systemic disorders. Moreover, the important role of the multidisciplinary cooperation to improve and sustain management of patients affected with eclectic ocular comorbidities and/or systemic disorders with eye repercussion is specifically addressed. This review intends to shed light on these topics to help in making opportune diagnosis and appropriately managing the affected patients.

PMID: 27051666 [PubMed - in process] PMCID: PMC4808667

Br J Ophthalmol. 2016 Apr 4. [Epub ahead of print]

Associations between obstructive sleep apnoea, primary open angle glaucoma and age-related macular degeneration: record linkage study.

Keenan TD, Goldacre R, Goldacre MJ.

BACKGROUND: Primary open angle glaucoma (POAG) is thought to be associated with obstructive sleep apnoea (OSA) but previous studies are conflicting and have methodological limitations. This potential relationship has implications for investigation and treatment strategies, and may provide insights into

disease pathogenesis. The relationship between OSA and age-related macular degeneration (AMD) is unknown.

METHODS: A sleep apnoea cohort of 67 786 people was constructed from linked English hospital episode statistics (1999-2011). We compared this cohort with a reference cohort (2 684 131 people) for rates of subsequent POAG and AMD. A POAG cohort (comprising 87 435 people) and an AMD cohort (248 408 people) were also constructed and compared with the reference cohort for rates of subsequent sleep apnoea. All analyses were restricted to people aged 55 and over and, within this age range, were age standardised using 5-year age groups.

RESULTS: Risk of POAG following sleep apnoea was not elevated: the rate ratio for POAG was 1.01 (95% CI 0.85 to 1.19). Similarly, the risk of sleep apnoea following POAG was not elevated: the rate ratio was 1.00 (0.86 to 1.17). These findings held true across subgroup analysis according to sex and age group. By contrast, the risk of AMD following sleep apnoea was significantly elevated, with rate ratio 1.44 (1.32 to 1.57).

CONCLUSIONS: Although plausible mechanisms exist to consider a link between OSA and POAG, the two conditions are not positively associated. This holds true in either temporal direction. By contrast, OSA is positively associated with AMD. While potential confounding factors may contribute, obesity does not appear sufficient to explain this association.

PMID: 27044342 [PubMed - as supplied by publisher]

Diet, lifestyle & low vision

Nutrients. 2016 Apr 5;8(4).

Resveratrol and Ophthalmic Diseases.

Abu-Amero KK, Kondkar AA, Chalam KV.

Abstract: Resveratrol, a naturally occurring plant polyphenol found in grapes, is the principal biologically active component in red wine. Clinical studies have shown that resveratrol due to its potent anti-oxidant and anti-inflammatory properties are cardio-protective, chemotherapeutic, neuroprotective, and display anti-aging effects. Oxidative stress and inflammation play a critical role in the initiation and progression of age-related ocular diseases (glaucoma, cataract, diabetic retinopathy and macular degeneration) that lead to progressive loss of vision and blindness. In vitro and in vivo (animal model) experimental studies performed so far have provided evidence for the biological effects of resveratrol on numerous pathways including oxidative stress, inflammation, mitochondrial dysfunction, apoptosis, pro-survival or angiogenesis that are implicated in the pathogenesis of these age-related ocular disorders. In this review, we provide a brief overview of current scientific literature on resveratrol, its plausible mechanism(s) of action, its potential use and current limitations as a nutritional therapeutic intervention in the eye and its related disorders.

PMID: 27058553 [PubMed - as supplied by publisher]

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