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MD Research News

Issue 230

Monday 4 May, 2015

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Drug treatment

Retina. 2015 Apr 29. [Epub ahead of print]

THE INFLUENCE OF VITREOMACULAR ADHESION ON OUTCOMES AFTER AFLIBERCEPT THERAPY FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

McKibbin MA, Suter CA, Willis TA.

PURPOSE: To evaluate the influence of vitreomacular attachment on outcomes after intravitreal aflibercept for neovascular age-related macular degeneration.

METHODS: In a prospective case series, eyes with neovascular age-related macular degeneration were treated with intravitreal aflibercept, given as 3 consecutive monthly injections, followed by further injection every 2 months. Spectral domain optical coherence tomography images were reviewed at each visit to determine the attachment of the posterior hyaloid. Best-corrected visual acuity and retinal thickness were also recorded. Outcomes at Months 2 and 6 were compared between the eyes with persistent vitreomacular attachment (Stage 1) and those with posterior vitreous detachment (Stages 2 or 3 PVD) at baseline.

RESULTS: At baseline, 30 eyes had Stage 1 PVD and 63 eyes had either Stage 2 or 3 PVD. Although there was a trend for both greater visual acuity gains and reductions in retinal thickness for the eyes with Stages 2 or 3 PVD, this failed to reach significance. Baseline visual acuity and age were negatively associated with visual acuity change, and baseline retinal thickness alone was associated with retinal thickness change.

CONCLUSION: Visual acuity, retinal thickness, and age at the baseline examination, but not PVD status, are associated with functional and anatomical outcomes after intravitreal aflibercept for neovascular age-related macular degeneration.

PMID: 25932561 [PubMed - as supplied by publisher]

BMC Ophthalmol. 2015 Apr 30;15(1):44. [Epub ahead of print]

Intravitreal aflibercept (Eylea) injection for cystoid macular edema secondary to retinitis pigmentosa - a first case report and short review of the literature.

Moschos MM, Moustafa GA.

BACKGROUND: Cystoid macular edema (CME) in retinitis pigmentosa (RP) has been managed in several ways as documented in the literature, with little success, though. The aim of our study was to report for the first time in literature the use of aflibercept in a patient with RP and CME.

CASE PRESENTATION: A 52-year-old man presented for blurred vision in his right eye. Best-corrected visual acuity (BCVA) was 3/10 in his right eye and 7/10 in his left eye. Physical examination and appropriate laboratory tests lead to the diagnosis of bilateral RP with CME in the right eye. Retinal thickness in the foveal area of the right eye was 631 µm. The patient was treated with a single intravitreal injection of 0.05 ml/0.5 mg aflibercept. One month later, BCVA of the right eye increased to 4/10, while BCVA of the left eye was unchanged. RT in the right eye decreased to 129 µm. Multifocal electroretinogram response did not improve, yet peaks were better-shaped and no areas of eccentral vision were present. Three and six months after injection, these improvements were maintained.

CONCLUSION: This first-reported case indicates that intravitreal aflibercept injection for addressing CME in RP seems to be an effective treatment.

PMID: 25925748 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2015 Mar;90 Suppl 1:29-34.

Management of aflibercept in routine clinical practice. [Article in English, Spanish]

Cabrera López F.

Abstract: Aflibercept is a new anti-vegf drug that, unlike ranibizumab and bevacizumab blocks both vegf-A and placental growth factor. Moreover, it binds with much greater strength and affinity to human vegf-A 165 than other endogenous vegf receptors, conferring it with a more extended effect and allowing a lower frequency of intravitreal injections.33-35 This facilitates the adoption of fixed treatment regimens other than monthly or individual regimens such as "treat and extend". Aflibercept is indicated for the treatment of neovascular (exudative) age-related macular degeneration (armd), visual alteration due to macular edema secondary to central retinal vein occlusion (crvo) and visual alteration due to diabetic macular edema (dme). The present article reviews the management of aflibercept in routine clinical practice, based on the specifications of its new core data sheet, which includes all the therapeutic indications in which its use has been approved and evaluating the distinct alternatives and treatment regimens after the initial loading doses.

PMID: 25925049 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2015 Mar;90 Suppl 1:24-28.

New perspectives in the approach to diabetic macular edema. Aflibercept therapy. [Article in English, Spanish]

Ruiz-Moreno JM.

Abstract: The VISTA and VIVID trials were conducted to compare the safety and efficacy of two intravitreal injection (IVI) regimens of aflibercept versus macular laser photocoagulation for the treatment of diabetic macular edema (DME). These double-masked, phase III clinical trials randomized (461/402) patients with DME to receive either 2mg aflibercept IVI every 4 weeks (2q4) or 2mg aflibercept IVI every 8 weeks (2q8) after 5 initial monthly doses vs macular laser photocoagularion. The primary efficacy endpoint was the mean change in best corrected visual acuity (BCVA) from baseline to week 52. Secondary efficacy endpoints were the change in central retinal thickness (CRT), the proportion of patients who gained ≥10 amd ≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters, and the change in the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) in near and distance vision. The mean BCVA gains in the 2q4 and 2q8 groups versus the laser group were 12.5 and 10.7 versus 0.2 letters ($p<0.0001$) in VISTA, and 10.5 and 10.7 versus 1.2 letters ($p<0.0001$) in VIVID. The proportions of patients gaining ≥ 15 letters and the proportion of patients with an improvement of > 2 levels in the severity of diabetic retinopathy was significant in the treatment groups versus the laser group. Mean reductions in CRT in the 2q4 and 2q8 groups vs the laser group were 185.9 and 183.1 versus 73.3 µm ($p<0.0001$) in VISTA, and 195.0 and 192.4

versus 66.2 µm (p<0.0001) in VIVID. The incidences of ocular and nonocular adverse events were similar in all groups. In conclusion, IIV aflibercept demonstrated statistically significant superiority in improvement in BCVA and reduction in DME over laser, with similar efficacy in the 2q4 and 2q8 groups in VISTA and VIVID.

PMID: 25925048 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2015 Mar;90 Suppl 1:15-23.

New perspectives in the approach to central retinal vein oclusion. [Article in English, Spanish]

Figueroa MS.

OBJECTIVE: The copernicus and galileo trials were designed to evaluate the safety and efficacy of intravitreal injection of 2mg of aflibercept in the treatment of macular edema secondary to central retinal vein occlusion.

MATERIAL AND METHOD: Two phase III randomized, double-masked trials: copernicus in North America (188 patients) and galileo in Europe and Asia (177 patients). In copernicus, the patients in the treatment group received monthly injections of 2mg aflibercept for 6 months and later continued with strict PRN treatment with monthly follow-up every 6 months and with a minimum of 3-monthly follow up for 1 year. Patients in the placebo group could receive treatment after the sixth month, with similar treatment regimens and follow-up to the treatment group. In contrast, in galileo, the placebo group received no PRN treatment until 1 year of follow-up and during the first 6 months, followup visits were bi-monthly.

RESULTS: The treatment group in copernicus showed a mean improvement of 13 letters versus the placebo group (1.5 letters) at week 100 of follow-up. In galileo, the mean best corrected visual acuity at 76 weeks were 13.7 and 6.6 in the treatment and placebo groups, respectively.

CONCLUSIONS: Early treatment with intravitreal aflibercept in achieves better results than when treatment is delayed by 6 months or 1 year. The visual benefits obtained with the drug are affected by the reduction in the frequency of monitoring during follow-up.

PMID: 25925047 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2015 Mar;90 Suppl 1:11-14.

New perspectives in the approach to age-related macular degeneration. [Article in English, Spanish]

Gallego-Pinazo R, Zapata MA.

Abstract: The approval of aflibercept for the neovascular form of age-related macular degeneration has opened up the possibility of treating patients with fewer injections, since the drug can be administered once every two months. Aflibercept can also be used as rescue therapy in patients with suboptimal response to other antiangiogenic treatments. The present study reviews the scientific evidence on aflibercept, both in treatment-naïve patients and in those with an unsatisfactory response to conventional treatments.

PMID: 25925046 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2015 Mar;90 Suppl 1:3-5.

Role of VEGF in diseases of the retina. [Article in English, Spanish]

Barquet LA.

Abstract: Angiogenesis is the process through which new blood vessels are formed, based on preexisting vessels, and is the paradigm of diseases such as cancer and exudative ageassociated macular degeneration (ARMD).1,2 Several proangiogenic factors have been identified, such as vascular endothelial growth factor (VEGF), especially VEGF-A, which activates endothelial cells and promotes cell proliferation, migration, and an increase in vascular permeability.3 VEGF is also involved in the etiopathogenesis of other retinal diseases, such as diabetic macular edema and macular edema secondary to retinal vein occlusion. Likewise, there is increasing evidence that placental growth factor (PIGF) acts recepsynergetically with VEGF in promoting these diseases. Currently, the main treatment for these diseases are the anti-VEGF drugs, aflibercept, ranibizumab and bevacizumab. These agents differ in their molecular structure and mechanism of action.

PMID: 25925044 [PubMed - as supplied by publisher]

Retina. 2015 Apr 25. [Epub ahead of print]

EFFECT OF PEGAPTANIB AND RANIBIZUMAB ON PLASMA AND VITREOUS HOMOCYSTEINE IN PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION.

Manresa N, Mulero J, Losada M, Zafrilla P.

PURPOSE: To investigate homocysteine (Hcy) concentration in the blood plasma and the vitreous in patients with exudative age-related macular degeneration receiving intravitreal anti-vascular endothelial growth factor therapy.

METHODS: Plasma Hcy and vitreous Hcy levels were analyzed in 73 exudative age-related macular degeneration patients (50.7% received pegaptanib 0.3 mg and 50.3% received ranibizumab 0.5 mg) and compared with 80 controls and 40 patients with idiopathic epiretinal membranes, respectively. Homocysteine concentration was measured by immunonephelometric particle test, and it was determined before and after antiangiogenic therapy.

RESULTS: The mean Hcy concentrations (±SD) of blood plasma and vitreous were 13.0 ± 4.2 μmol/L and 1.00 ± 0.3 μmol/L in patients treated with pegaptanib; in ranibizumab group, they were 12.8 ± 2.5 μmol/L and 1.4 ± 0.6 μmol/L, respectively. The results of plasma and vitreous Hcy indicated statistically significant differences between exudative age-related macular degeneration patients and control groups (P = 0.03 and P = 0.02). After 6 months with both intravitreal therapies, the plasma and vitreous Hcy concentrations did not change significantly (P = 0.1).

CONCLUSION: Pegaptanib and ranibizumab did not increase the plasma or vitreous Hcy concentrations.

PMID: 25923955 [PubMed - as supplied by publisher]

J Clin Pharm Ther. 2015 Apr 30. [Epub ahead of print]

Ischaemic stroke after exposure to aflibercept: interaction with vitamin K antagonist and/or direct pharmacodynamic effect?

Thorel J, Civade E, Quintyn JC, Cestac P, Montastruc JL, Bagheri H.

WHAT IS KNOWN AND OBJECTIVE: zVascular endothelial growth factor (VEGF) proteins are involved in the regulation of vascular endothelium, and their inhibition led to the development of a number of drugs used for malignancies or exudative neo-vascular age-related macular degeneration (AMD).

CASE SUMMARY: We report a case of ischemic stroke in an 87-year-old woman having received intravitreal aflibercept, a new anti-VEGF for AMD. She had been treated with ranibizumab since 2007. In 2013, ranibizumab was replaced with aflibercept, followed by a decrease in the International Normalized Ratio, complicated by a stroke a few days later. The rechallenge was positive.

WHAT IS NEW AND CONCLUSION: A potential time-dependent interaction between aflibercept and VKA antagonist and/or a direct effect of aflibercept may have contributed to the occurrence of the ischaemic stroke. Currently available data suggest some pharmacokinetic and pharmacodynamic effects of aflibercept by explaining its pro-thrombotic profile.

PMID: 25930164 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Retina. 2015 Apr 29. [Epub ahead of print]

MULTIMODAL VISUAL FUNCTION TESTING IN EYES WITH NONEXUDATIVE AGE-RELATED MACULAR DEGENERATION.

Ooto S, Suzuki M, Vongkulsiri S, Sato T, Spaide RF.

PURPOSE: To investigate the interactions among drusen type and multimodal vision testing in eyes with nonexudative age-related macular degeneration.

METHODS: Fifty-one eyes of 39 patients with nonexudative age-related macular degeneration underwent fundus imaging including spectral domain optical coherence tomography, color fundus photograph, and autofluorescence imaging, each of which was graded by 2 masked readers. Multimodal vision testing included visual acuity using the Early Treatment Diabetic Retinopathy Study protocol refraction, contrast sensitivity, and microperimetry.

RESULTS: Generalized estimating equation modeling showed that the significant predictors of contrast sensitivity was the presence of pseudodrusen (P = 0.012) and refractive error (P = 0.028). The presence of pseudodrusen inversely correlated with contrast sensitivity. The significant predictors of parafoveal microperimetry score were area of confluent hypoautofluorescence (P = 0.026) and the presence of pseudodrusen (P = 0.027). Both of them showed an inverse correlation with microperimetry score. The only significant predictor of macular microperimetry score was the presence of pseudodrusen (P = 0.004), which showed an inverse correlation with microperimetry score.

CONCLUSION: The analysis of predictors of the visual function highlights the importance of pseudodrusen. Pseudodrusen are not only the risk factor of late age-related macular degeneration but also affect visual function. Recognition of this problem is important for low-vision rehabilitation and therapeutic strategies for late age-related macular degeneration.

PMID: 25932557 [PubMed - as supplied by publisher]

Retina. 2015 Apr 29. [Epub ahead of print]

PHASE II, RANDOMIZED, PLACEBO-CONTROLLED, 90-DAY STUDY OF EMIXUSTAT HYDROCHLORIDE IN GEOGRAPHIC ATROPHY ASSOCIATED WITH DRY AGE-RELATED MACULAR DEGENERATION.

Dugel PU, Novack RL, Csaky KG, Richmond PP, Birch DG, Kubota R.

PURPOSE: This study assessed the safety, tolerability, and pharmacodynamics of emixustat hydrochloride (ACU-4429), a novel visual cycle modulator, in subjects with geographic atrophy associated with dry age-related macular degeneration.

METHODS: Subjects were randomly assigned to oral emixustat (2, 5, 7, or 10 mg once daily) or placebo (3:1 ratio) for 90 days. Recovery of rod photoreceptor sensitivity after a photobleach was measured by electroretinography. Safety evaluations included analysis of adverse events and ophthalmic examinations.

RESULTS: Seventy-two subjects (54 emixustat and 18 placebo) were evaluated. Emixustat suppressed rod photoreceptor sensitivity in a dose-dependent manner. Suppression plateaued by Day 14 and was reversible within 7 days to 14 days after drug cessation. Most systemic adverse events were not considered treatment related. Dose-related ocular adverse events (chromatopsia, 57% emixustat vs. 17% placebo and delayed dark adaptation, 48% emixustat vs. 6% placebo) were mild to moderate in severity, and the majority resolved on study or within 7 days to 14 days after study drug cessation. Reversibility of these adverse events with long-term administration, however, is undetermined.

CONCLUSION: In this Phase II study, emixustat produced a dose-dependent reversible effect on rod function that is consistent with the proposed mechanism of action. These results support further testing of emixustat for the treatment of geographic atrophy associated with dry age-related macular degeneration.

PMID: 25932553 [PubMed - as supplied by publisher]

BMC Ophthalmol. 2015 Apr 28;15(1):43. [Epub ahead of print]

Disappearance of soft drusen and subsequent development of choroidal neovascularization following macular hole surgery: a case report.

Lee JH, Lee T, Lee SC, Lee CS.

BACKGROUND: Drusen are important risk factor for neovascular age-related macular degeneration (AMD) and have a dynamic nature as they can enlarge, newly form, or disappear over time. There have been few reports on drusen regression or choroidal neovascularization (CNV) development after macular hole surgery. We report, to our knowledge, the first case of both drusen regression and subsequent CNV development within 7 months of successful macular hole surgery.

CASE PRESENTATION: A 73-year-old woman presented with a stage 3 full-thickness macular hole and large, confluent soft macular drusen in the right eye and a neovascular age-related macular degeneration (AMD) in the fellow eye. Four months after the successful macular hole surgery, significant regression of drusen was seen, especially in the temporal area to the fovea. Three months later, the patient developed CNV and her best-corrected visual acuity decreased to 20/100, despite further regression of macular drusen.

CONCLUSIONS: Macular hole patients with macular soft drusen need to be carefully followed up after surgery for possible drusen regression and CNV development.

PMID: 25928705 [PubMed - as supplied by publisher]

Lab Chip. 2015 Apr 29. [Epub ahead of print]

Monitoring VEGF levels with low-volume sampling in major vision-threatening diseases: age-related macular degeneration and diabetic retinopathy.

Hsu MY, Chen SJ, Chen KH, Hung YC, Tsai HY, Cheng CM.

Abstract: The purpose of this article is to demonstrate the capacity of paper-based ELISA (P-ELISA) to monitor VEGF in patients requiring treatment for vision-threatening diseases. The most commonly encountered vision-threatening diseases are age-related macular degeneration (AMD) and diabetic retinopathy (DR), both of which may require short-term or life-long anti-VEGF injection treatment therapy. Accurate measurement of VEGF concentration in aqueous humor can provide significant and timely information to diagnose the disease state. Adequate and precise therapy may consequently be provided. At odds with conventional diagnostic approaches is the fact that a maximum of only 200 microliters of aqueous humor can be safely removed from the eye for testing. Fortunately, new diagnostic platforms, such as P-ELISA, require only minute volumes, i.e., approximately 2 microliters per test "well" and approximately 40

microliters total to quantify VEGF levels, and the testing process takes less than an hour. Thus, point-of-care (POC) diagnostics, such as P-ELISA, should be examined and improved upon as needed in order to develop an efficient tool for outpatient clinics and others to obtain semi-quantitative results that might facilitate accurate dosing of anti-VEGF treatment and delay or prevent the progression of AMD and DR.

PMID: 25923964 [PubMed - as supplied by publisher]

Retina. 2015 Apr 25. [Epub ahead of print]

WEDGE-SHAPED SUBRETINAL HYPOREFLECTIVITY IN GEOGRAPHIC ATROPHY.

Querques G, Capuano V, Frascio P, Zweifel S, Georges A, Souied EH.

PURPOSE: To describe wedge-shaped subretinal hyporeflectivity, a peculiar spectral domain optical coherence tomography finding in geographic atrophy (GA) areas of atrophic age-related macular degeneration.

METHODS: We reviewed the charts of consecutive patients with GA who presented between January 2012 and December 2013. A standardized imaging protocol was performed in all patients, which included blue fundus autofluorescence, and spectral domain optical coherence tomography.

RESULTS: Wedge-shaped subretinal hyporeflective lesions were found in 12 of 161 included eyes (11 of 94 consecutive patients, 6 males/5 females, mean age 79.6 ± 9.3 years). On spectral domain optical coherence tomography, regions immediately adjacent to the wedge-shaped subretinal hyporeflective lesions were characterized by absence of the hyporeflective outer nuclear layer, the hyperreflective external limiting membrane, the ellipsoid zone, the interdigitation zone, and the retinal pigment epithelium. On "en face" images, they appeared as round-oval hyporeflectivities delimited by hyperreflective borders, which we interpreted as the outer plexiform layer. Mean GA area was significantly larger in eyes with as compared with eyes without wedge-shaped subretinal hyporeflective lesions. Overall, the dimensions of the wedge-shaped subretinal hyporeflective lesions did not change after a mean of ∼15 months.

CONCLUSION: Wedge-shaped subretinal hyporeflectivity, a previously unreported peculiar finding in GA areas of atrophic age-related macular degeneration eyes, appears delimited internally by the hyperreflective outer plexiform layer and externally by the hyperreflective Bruch membrane. These lesions, which are detected in eyes with large GA (even though stable over time), should be recognized and distinguished from subretinal fluid (and other exudative signs of age-related macular degeneration) because their presence should not require prompt treatment.

PMID: 25923956 [PubMed - as supplied by publisher]

Open Ophthalmol J. 2015 Mar 31;9:36-40. eCollection 2015.

The causes of hyperreflective dots in optical coherence tomography excluding diabetic macular edema and retinal venous occlusion.

Turgut B, Yildirim H.

PURPOSE: To investigate the causes of hyperreflective dots (HRDs) in spectral domain optical coherence tomography (OCT) excluding diabetic macular edema (DME) and RVO (retinal vein occlusion).

PATIENTS AND METHODS: The medical records of 56 patients with HRDs documented by OCT were reviewed retrospectively. The patients with DME and RVO were excluded from the study in order to prevent misdiagnosing hard exudates or HRDs. The causes, unilaterality or bilaterality of HRD and demographic properties of the patients with HRD were evaluated.

RESULTS: Sixty four eyes of 56 patients having HRDs were included in this study. Of the patients with HRD, 17 (30.36%) were women and 39 (69.64%) were men. The ages of patients were between 13 to 84

years (median 60.18 years). The causes of HRD were as follows: papilledema in 4 eyes (6.25%), active neovascular age related macular degeneration (AMD) in 33 eyes (51.56%), familial dominant drusen in 2 eyes (3.13%), central serous chorioretinopathy in 19 eyes (29.69%) and commotio retina in 2 eyes (3.13%), choroidal folds in one eye (1.56%), branch retinal artery occlusion in one eye (1.56%), central retinal artery occlusion in one patient (1.56%) and Best vitelliform macular dystrophy in one eye (1.56%). The most common cause of HRD was AMD. The causes of HRDs in both eyes were AMD and papilledema.

CONCLUSION: The most common causes of HRDs excluding DME and RVO seem as active exudative AMD. The presence of HRDs in retinal diseases might affect the decisions and the results of the treatment and the prognosis of diseases.

PMID: 25926902 [PubMed] PMCID: PMC4407005

Pathogenesis

PLoS One. 2015 Apr 29;10(4):e0125631. eCollection 2015.

A comparison of some organizational characteristics of the mouse central retina and the human macula.

Volland S, Esteve-Rudd J, Hoo J, Yee C, Williams DS.

Abstract: Mouse models have greatly assisted our understanding of retinal degenerations. However, the mouse retina does not have a macula, leading to the question of whether the mouse is a relevant model for macular degeneration. In the present study, a quantitative comparison between the organization of the central mouse retina and the human macula was made, focusing on some structural characteristics that have been suggested to be important in predisposing the macula to stresses leading to degeneration: photoreceptor density, phagocytic load on the RPE, and the relative thinness of Bruch's membrane. Light and electron microscopy measurements from retinas of two strains of mice, together with published data on human retinas, were used for calculations and subsequent comparisons. As in the human retina, the central region of the mouse retina possesses a higher photoreceptor cell density and a thinner Bruch's membrane than in the periphery; however, the magnitudes of these periphery to center gradients are larger in the human. Of potentially greater relevance is the actual photoreceptor cell density, which is much greater in the mouse central retina than in the human macula, underlying a higher phagocytic load for the mouse RPE. Moreover, at eccentricities that correspond to the peripheral half of the human macula, the rod to cone ratio is similar between mouse and human. Hence, with respect to photoreceptor density and phagocytic load of the RPE, the central mouse retina models at least the more peripheral part of the macula, where macular degeneration is often first evident.

PMID: 25923208 [PubMed - in process]

Genetics

Biomed Res Int. 2015;2015:940864. Epub 2015 Apr 2.

Identification of Novel Mutations in ABCA4 Gene: Clinical and Genetic Analysis of Indian Patients with Stargardt Disease.

Battu R, Verma A, Hariharan R, Krishna S, Kiran R, Jacob J, Ganapathy A, Ramprasad VL, Kumaramanickavel G, Jeyabalan N, Ghosh A.

Abstract: Stargardt disease (STGD) is the leading cause of juvenile macular degeneration associated with progressive central vision loss, photophobia, and colour vision abnormalities. In this study, we have described the clinical and genetic features of Stargardt patients from an Indian cohort. The next generation sequencing was carried out in five clinically confirmed unrelated patients and their family members using a

gene panel comprising 184 retinal specific genes. Sequencing results were analyzed by read mapping and variant calling in genes of interest, followed by their verification and interpretation. Genetic analysis revealed ABCA4 mutations in all of the five unrelated patients. Among these, four patients were found with compound heterozygous mutations and another one had homozygous mutation. All the affected individuals showed signs and symptoms consistent with the disease phenotype. We report two novel ABCA4 mutations in Indian patients with STGD disease, which expands the existing spectrum of disease-causing variants and the understanding of phenotypic and genotypic correlations. Screening for causative mutations in patients with STGD using panel of targeted gene sequencing by NGS would be a cost effective tool, might be helpful in confirming the precise diagnosis, and contributes towards the genetic counselling of asymptomatic carriers and isolated patients.

PMID: 25922843 [PubMed - in process] PMCID: PMC4398921

Gene. 2015 Apr 25. [Epub ahead of print]

Associations of the G1961E and D2177N variants in ABCA4 and the risk of age-related macular degeneration.

Zhang R, Wang LY, Wang YF, Wu CR, Lei CL, Wang MX, Ma L.

OBJECTIVE: The aim of this study was to identify the relationship between G1961E and D2177N variants in the ABCA4 gene with AMD susceptibility.

DESIGN AND METHODS: All eligible studies published up to October 2014 were obtained from MEDLINE, EMBASE, and ISI Web of Science. The pooled odds ratio (OR) with 95% confidence intervals (CIs) was calculated to evaluate the strength of this association.

RESULTS: Twenty-four studies enrolling 4580 AMD cases and 5180 controls were identified. Both G1961E (OR=3.22, 95% CI: 1.74-5.95) and D2177N (OR=2.36, 95% CI: 1.41-3.93) variations showed significant associations with increased risk of AMD. In addition, a more significant relationship in the D2177N mutation with increased risk for AMD was found in Americans (OR=4.31, 95% CI: 1.90-9.73), while no association was demonstrated in Europeans. For Asians, no carriers of the risk factor A allele in either variant were detected in any of AMD patients and control subjects.

CONCLUSIONS: Significant evidence was found for a relationship between the G1961E and D2177N variants in ABCA4 with increased susceptibility to AMD, specifically for Americans. However, large-scale studies are still required to further validate these findings in different ethnicities.

PMID: 25921964 [PubMed - as supplied by publisher]

Diet, lifestyle & low vision

PLoS One. 2015 May 1;10(5):e0125394. eCollection 2015.

Age-Related Macular Degeneration Is Associated with Less Physical Activity among US Adults: Cross-Sectional Study.

Loprinzi PD, Swenor BK, Ramulu PY.

BACKGROUND: We have a limited understanding of the effects of age-related macular degeneration (AMD) on physical activity (PA), and we have no prevalence estimates of the daily movement patterns among Americans with AMD. Therefore, we examined the association between AMD and PA and provided estimates of the daily movement patterns of Americans with AMD.

METHODS: Data from the 2005-2006 National Health and Nutrition Examination Survey were used,

including 1,656 adults (40-85 yrs). Retinal imaging was performed to classify individuals as no AMD, early AMD, or late AMD. Participants wore an ActiGraph 7164 accelerometer for 7 days to measure PA behavior.

RESULTS: 93.2% of participants with late AMD were in the least desirable group (not sufficiently active and having a negative light intensity-sedentary behavior balance). After adjustments (including age), participants with late AMD, as compared to those with no AMD, engaged in 50% less moderate-to-vigorous physical activity (MVPA) (RR = 0.50; 95% CI: 0.28-0.90). When visual acuity was entered into the model along with the other covariates, the association between late AMD and MVPA was no longer significant (RR = 0.54; 95% CI: 0.29-1.01), suggesting that visual acuity may partially mediate this relationship.

CONCLUSIONS: Individuals with late AMD engage in very little moderate-to-vigorous physical activity. Visually acuity, in part, explains the relationship between late AMD and PA.

PMID: 25933421 [PubMed - in process]

Optom Vis Sci. 2015 Apr 30. [Epub ahead of print]

Fear of Falling in Vision Impairment.

White UE, Black AA, Wood JM, Delbaere K.

Abstract: Falls are the leading cause of injury-related morbidity and mortality among older adults. In addition to the resulting physical injury and potential disability after a fall, there are also important psychological consequences, including depression, anxiety, activity restriction, and fear of falling. Fear of falling affects 20 to 43% of community-dwelling older adults and is not limited to those who have previously experienced a fall. About half of older adults who experience fear of falling subsequently restrict their physical and everyday activities, which can lead to functional decline, depression, increased falls risk, and reduced quality of life. Although there is clear evidence that older adults with visual impairment have higher falls risk, only a limited number of studies have investigated fear of falling in older adults with visual impairment and the findings have been mixed. Recent studies suggest increased levels of fear of falling among older adults with various eye conditions, including glaucoma and age-related macular degeneration, whereas other studies have failed to find differences. Interventions, which are still in their infancy in the general population, are also largely unexplored in those with visual impairment. The major aims of this review were to provide an overview of the literature on fear of falling, its measurement, and risk factors among older populations, with specific focus on older adults with visual impairment, and to identify directions for future research in this area.

PMID: 25930978 [PubMed - as supplied by publisher]