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MD Research News

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Drug treatment

Graefes Arch Clin Exp Ophthalmol. 2011 Apr 15. [Epub ahead of print]

Early visual impacts of optical coherence tomographic parameters in patients with age-related macular degeneration following the first versus repeated ranibizumab injection.

Sayed KM, Naito T, Nagasawa T, Katome T, Mitamura Y.

The Department of Ophthalmology and Visual Neuroscience, Institute of Health Biosciences, The University of Tokushima Graduate School, 3-18-15 Kuramoto-cho, Tokushima, 770-8503, Japan.

BACKGROUND: The aim of this study is to evaluate the early visual impacts of various optical coherence tomographic (OCT) parameters after the first versus repeated intravitreal ranibizumab injection in patients with exudative age-related macular degeneration (AMD).

METHODS: A retrospective comparative case series study was conducted on 20 eyes of 18 consecutive patients who received intravitreal ranibizumab injection for exudative AMD either for the first time (group 1; n = 8) with no prior anti-vascular endothelial growth factor (anti-VEGF) injection in the same or fellow eye, or for repeated times during the course of monthly injected ranibizumab (group 2; n = 12 eyes). The following baseline and 1 month post-injection data was collected for both groups and compared: best-corrected visual acuity (BCVA), qualitative and quantitative OCT parameters including: foveal thickness, foveal volume (central 1-mm circle), retinal volume at 3- and 5-mm central circles, retinal pigment epithelium (RPE) elevation, type of fluid collections, and type of AMD lesion. The size of the fluid and fibrovascular lesion (FVL) areas were measured using manual delineation and automatic calculation of the device. We made correlations between the post-injection visual acuity (VA) and each of post-injection OCT parameters in both groups and these were the main outcome measures.

RESULTS: In group 1, there was a strong correlation between post-injection logarithm of minimum angle of resolution (logMAR) BCVA and each of the following: FVL size, foveal thickness, retinal volume at 3- and 5-mm central circles, RPE elevation, the size of the fluid area, and age of the patient ($r > 0.70$, $p < 0.05$), whereas in group 2; logMAR BCVA was strongly correlated only with foveal volume ($r = 0.74$, $p = 0.01$). Multivariate analysis showed that post-injection FVL size ($r (2) = 0.69$) and foveal volume ($r (2) = 0.55$) were the most important factors for VA 1 month following the initial and repeated ranibizumab injection, respectively.

CONCLUSIONS: The size of FVL and foveal volume showed a significant correlation with VA in AMD patients shortly after the first and repeated ranibizumab injection, respectively. Further studies with larger sample sizes are needed in order to support these results.

PMID: 21494878 [PubMed - as supplied by publisher]

Adv Ther. 2011 Mar 12. [Epub ahead of print]

The dexamethasone drug delivery system: Indications and evidence.

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INTRODUCTION: The Ozurdex® (Allergan Inc., Irvine, CA, USA) dexamethasone drug delivery system (DDS) was recently developed as a biodegradable intravitreal implant to provide sustained delivery of 700 µg of preservativefree dexamethasone to the retina and vitreous, and is approved by the United States Food and Drug Administration (FDA) for the treatment of macular edema associated with retinal vein occlusion, as well as for noninfectious posterior uveitis. This review summarizes the rationale behind the development of the dexamethasone DDS, evidence for its use in various clinical scenarios, and compares its efficacy to other available treatment options.

METHODS: Published data regarding the dexamethasone DDS as well as unpublished data that has been presented at national meetings were reviewed.

RESULTS: The dexamethasone DDS has evidence for efficacy in multiple clinical situations, including macular edema associated with retinal vein occlusion (RVO), macular edema associated with uveitis or Irvine-Gass syndrome, diabetic macular edema in vitrectomized eyes, persistent macular edema, noninfectious vitritis, and as adjunctive therapy for age-related macular degeneration. Safety concerns include cataract formation and intraocular pressure elevation that is most often temporary and amenable to medical management.

CONCLUSIONS: The dexamethasone DDS is one of the most recent additions to the armamentarium against macular edema, and is intriguing for its potency, dose consistency, potential for extended duration of action, and favorable safety profile. Early evidence shows clinical utility for several conditions, the most well established being for macular edema associated with RVO. Future studies and, in particular, head-to-head comparisons with other treatment modalities will elucidate the precise role for the dexamethasone DDS in clinical practice.

PMID: 21494891 [PubMed - as supplied by publisher]

Eye (Lond). 2011 Apr;25(4):399-401.

Ranibizumab: a medical treatment that requires surgical administration.

Amoaku WM.

Queen's Medical Centre, University Hospital, Nottingham, UK.

PMID: 21490696 [PubMed - in process]

Int Wound J. 2011 Apr 12. doi: 10.1111/j.1742-481X.2011.00799.x. [Epub ahead of print]

Acute generalised exanthematous pustulosis following intravitreal Ranibizumab.

Bosanquet DC, Davies WL, May K, Harding KG, Patel GK.

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University, Heath Park, Cardiff CF14 4XN, UK GK Patel, MRCP, Department of Dermatology and Wound Healing, School of Medicine, Cardiff University, Heath Park, Cardiff CF14 4XN, UK.

Abstract

Acute generalised exanthematous pustulosis, or AGEP, is a well documented cutaneous drug reaction. It typically occurs within 48 hours of oral antibiotics, but can be caused by other medications and, occasionally, after viral infections. We present a case of AGEP following intravitreal injection of Ranibizumab, a monoclonal antibody vascular endothelial growth factor inhibitor.

PMID: 21486393 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2011 Apr 6. pii: 40A0A7CC-15D6-4B69-BBA6-0FE9D8042F75. [Epub ahead of print]

Ranibizumab in retinal angiomatous proliferation (RAP): influence of RAP stage on visual outcome.

Reche-Frutos J, Calvo-Gonzalez C, Pérez-Trigo S, Fernandez-Perez C, Donate-Lopez J, Garcia-Feijoo J.

Ophthalmology Department, Hospital Clinico San Carlos, Madrid - Spain.

Purpose: To evaluate the influence of retinal angiomatous proliferation (RAP) stage on visual and anatomic outcome after ranibizumab (Lucentis®).

Methods: This was a prospective study on consecutively diagnosed RAP eyes at the Hospital Clínico San Carlos, Madrid. Best-corrected visual acuity (BCVA) and optical coherence tomography (OCT) are performed monthly. Indocyanine green angiography (ICG) and fluorescein angiography (FA) are performed at baseline and every 3 months thereafter. A starting dose of a monthly ranibizumab injection in the first 3 months is followed by retreatment in case of intraretinal edema, subretinal fluid, or pigment epithelium detachment (PED) in OCT, increased leakage in FA, or a hot spot in ICG.

Results: A total of 53 eyes from 49 patients were included. The mean change in BCVA at 12 months was +7.3, +0.83, and -2.1 letters in stages IIA (21 cases), II B (18 cases), and III (14 cases), respectively. After adjusting the change in BCVA according to baseline BCVA, ß coefficient was -6.012 letters (p=0.025) in stage IIB and -9.762 letters (p=0.003) in stage III vs stage IIA. Four cases had a retinal pigment epithelium tear after injection of ranibizumab.

Conclusions: Patients in stage II without PED have a better visual and anatomic evolution than patients in stage II with PED and stage III.

PMID: 21484755 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2011 Apr;228(4):340-344. Epub 2011 Apr 11.

[Photodynamic Therapy in "Secondary Sick RPE Syndrome" after Repeated Intravitreal Injections of VEGF Inhibitors in Patients with Wet Age-Related Macular Degeneration.]

[Article in German]

Kloos P, Niederberger H, Valmaggia C.

Augenklinik, Kantonsspital, St. Gallen, Schweiz.

BACKGROUND: After repeated injections of VEGF inhibitors for wet AMD some patients show therapy-resistant isolated subretinal fluid (here named secondary sick RPE syndrome). The efficacy of photodynamic therapy was examined in these cases.

PATIENTS AND METHODS: A group of in total 18 patients with wet AMD (14 eyes with occult and 4 with minimal classic CNV) showed therapy-resistant isolated subretinal fluid after repeated intravitreal injections of VEGF inhibitors (bevacizumab or ranibizumab). These eyes were treated with photodynamic therapy with verteporfin. After PDT the need for further intravitreal injections of VEGF inhibitors and visual acuity was examined.

RESULTS: After a mean number of 7.1 injections of VEGF inhibitors (bevacizumab or ranibizumab), in 14 patients one PDT, in 4 patients two PDT were performed. Twelve of 18 patients showed complete resorption of subretinal fluid and needed no further intravitreal injections during a mean of 11.6 months (4 - 26) after PDT. Six patients needed a mean of 4.3 additional injections. Twelve of 18 patients showed stable visual acuity (± 5 letters ETDRS), 6 improved more than 5 letters while none of them showed visual loss.

CONCLUSIONS: In patients with wet AMD and isolated subretinal fluid after repeated injections of bevacizumab or ranibizumab photodynamic therapy could be an option to reduce the number of further injections and to stabilise visual acuity.

PMID: 21484643 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2011 Apr;228(4):391-394. Epub 2011 Apr 11.

Combined Cilioretinal Artery and Central Retinal Vein Occlusion Treated with a Single Injection of Ranibizumab.

Katsimpris JM, Theoulakis PE, Lepidas J, Livieratou A, Petropoulos IK.

PMID: 21484666 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2011 Apr;228(4):288-292. Epub 2011 Apr 11.

Intravitreal Ranibizumab in the Treatment of Predominantly Hemorrhagic Lesions in Exudative Age-Related Macular Degeneration.

Konstantinidis L, Mantel I, Zografos L, Ambresin A.

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BACKGROUND: Submacular hemorrhage is a manifestation of neovascular age-related macular degeneration (AMD) that has a very poor natural history leading to severe visual loss. We have evaluated the safety and efficacy of intravitreal ranibizumab in the treatment of predominantly hemorrhagic AMD.

PATIENTS AND METHODS: A retrospective study of patients with predominantly hemorrhagic AMD treated with intravitreal ranibizumab at the Jules Gonin Eye Hospital between December 2006 and December 2008 was undertaken. Baseline and monthly follow-up exams included visual acuity (VA), fundus exam and optical coherence tomography (OCT) while fluorescein and indocyanine green angiography were performed at least every three months.

RESULTS: The study included 8 eyes. The mean follow-up was 13 months (SD: 6.3). The mean number of intravitreal injections administered for each patient was 6.4 (SD: 2). 50 % of the patients demonstrated stable or improved VA. The size of hemorrhage at baseline was inversely correlated to the final VA (two-tailed p value = 0.038) and positively correlated to the final central macular thickness (two-tailed p value = 0.021). Anticoagulation treatment was inversely correlated to the time of hemorrhage resolution (two-tailed p value = 0.039).

CONCLUSIONS: Intravitreal ranibizumab may be an effective treatment for predominantly hemorrhagic lesions due to neovascular AMD.

PMID: 21484631 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2011 Apr;228(4):284-287. Epub 2011 Apr 11.

[Results of Ranibizumab Treatment for Choroidal Neovascularization Secondary to Pathological Myopia.]

[Article in German]

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PURPOSE: Choroidal neovascularization (CNV) secondary to pathological myopia (PM) occurs in up to 10 % of PM and the natural course often leads to a considerable deterioration of visual acuity. Treatment options like laser or PDT can stabilize visual acuity. Alternatives like ranibizumab are new treatment options that show very promising results. It was the aim of this analysis to evaluate the development of visual acuity and the number of injections needed in patients with myopia-associated secondary CNVs.

METHODS: We retrospectively analysed 10 eyes of 9 patients (7 women, 2 men, mean age: 66 years, SD 8.3; range: 54 - 78 years) treated with ranibizumab because of CNV secondary to PM. All eyes were treatment naïve. Criteria for re-treatment were loss of visual acuity and/ or activity in OCT or fluorescence angiography.

RESULTS: During the mean follow-up of 10 months (SD 6.1; range: 6 to 26 months) a mean of 2.5 (SD 1.6, range: 1 to 5) injections of ranibizumab was applied. The spherical equivalent was - 12 D (SD 4.8, range - 7,5 D to - 20.5 D). Previous to the first injection mean visual acuity was logMAR 0,64 (SD 0.20) (ETDRS: 52.8; SD: 11.4) and during the follow-up a mean of 3.4 lines (ETDRS: 16.5 letters) was gained (p = 0.008). After one month visual acuity improved to log MAR 0.47 (SD 0.1, p = 0.0012) (ETDRS: 61.7; SD: 6.5), after 3 months log MAR 0.38 (SD 0.1, p = 0.012) (ETDRS: 65.8; SD: 5.6) and after 6 months up to log MAR 0.35 (SD 0.1, p = 0.008) (ETDRS 67.3; SD 5.6). At the end of the follow-up visual acuity was log MAR 0.30 (SD 0.1) (ETDRS: 69.3; SD: 6.7).No patient experienced a loss of visual acuity. No ocular or systemic side effects were observed.

CONCLUSION: According to our results treatment of CNV secondary to PM with ranibizumab leads to a substantial improvement of visual acuity. It seems that successful treatment of CNV secondary to PM needs less anti-VEGF injections than the treatment of neovascularizations due to age-related macular degeneration. Anti-VEGF seems to be a promising alternative to PDT and laser photocoagulation in myopia -related CNV.

PMID: 21484630 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2011 May;22(3):152-8.

Ranibizumab versus bevacizumab for the treatment of neovascular age-related macular degeneration.

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PURPOSE OF REVIEW: This paper reviews the recent literature regarding the effectiveness, efficacy and safety of intravitreal bevacizumab as compared with ranibizumab for the treatment of neovascular age-related macular degeneration (nAMD).

RECENT FINDINGS: Numerous randomized clinical trials have demonstrated the safety and efficacy of ranibizumab for the treatment of nAMD. Bevacizumab, developed, labeled and approved for the

management of colorectal cancer, has been used off-label for the management of nAMD. However, given its lower cost and effectiveness, it is commonly used for many cases of nAMD. Recent clinical trials have demonstrated similar effectiveness between the two compounds in terms of visual acuity and central macular thickness. However, emerging data have suggested that these two compounds may have different ocular and systemic adverse event profiles; bevacizumab has been linked to both a higher risk of severe intraocular inflammation and a higher risk of incident arterial thromboembolic events. This incremental risk for both ocular and systemic adverse events may have an impact on the incremental cost-effectiveness ratio derived from health economic models that directly compare one anti-vascular endothelial growth factor (VEGF) compound to the other.

SUMMARY: Numerous clinical trials, including the Comparison of AMD Treatment Trial, are underway examining the comparative efficacy of ranibizumab versus bevacizumab for the treatment of nAMD. While these studies may demonstrate clinical noninferiority of one anti-VEGF compound over another, they may not be adequately powered to detect important differences in ocular and systemic safety. Large-scale, appropriately powered safety studies need to be conducted to evaluate differences in safety.

PMID: 21483262 [PubMed - in process]

Other treatment & diagnosis

Optom Vis Sci. 2011 Apr 7. [Epub ahead of print]

Measuring Visual Function in Age-Related Macular Degeneration with Frequency-Doubling (Matrix) Perimetry.

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PURPOSE: To determine the agreement between the Humphrey Matrix perimeter 10-2 test and the 10-2 Humphrey Field Analyzer (HFA) test when assessing visual function in patients with age-related macular degeneration (AMD).

METHODS: Forty-two eyes of 42 subjects with AMD (average 75.0 years, SD = 6.2: median visual acuity in logarithm of the minimum angle of resolution of 0.26, range, -0.12 to 1.04) were evaluated with the Matrix and HFA 10-2 visual field tests. Mean deviation (MD), pattern standard deviation, and test time were recorded. We calculated spatial concordance of individual test locations, being the proportion of spatially agreeing locations with identical classification (normal vs. abnormal, $p < 5\%$) on the pattern deviation plot. As multiple HFA stimuli overlapped with some Matrix locations, several criteria for grouping HFA data into locations were investigated.

RESULTS: Both MD and pattern standard deviation were significantly correlated for the two devices ($r = 0.79$ and $r = 0.80$, respectively, $p < 0.0001$). Using our standard criterion for abnormal HFA locations (≥50% stimuli abnormal), the median spatial concordance was 0.76, with 95% of tests giving a concordance of ≥0.59. A small, but significant, increase in concordance occurred when a stricter criterion (all stimuli abnormal at a location) was applied. Median fixation loss percentages were 7 and 0% for the HFA and Matrix, respectively. Visual acuity in logarithm of the minimum angle of resolution showed modest correlations with both defect depth (HFA MD: $r = 0.39$, $p < 0.0001$) and size of defect (number of abnormal points on the HFA: $r = 0.24$, $p < 0.0001$).

CONCLUSIONS: Using a simple metric to calculate spatial concordance, the Matrix 10-2 test quantifies the spatial extent of significant depression of the central visual fields in AMD in a manner similar to the HFA 10-

2. The spatial extent and depth of central visual field loss in AMD are only modestly predicted by visual acuity measurements.

PMID: 21478785 [PubMed - as supplied by publisher]

Retina. 2011 Apr 9. [Epub ahead of print]

PERIPHERAL AREAS OF NONPERFUSION IN TREATED CENTRAL RETINAL VEIN OCCLUSION AS IMAGED BY WIDE-FIELD FLUORESCEIN ANGIOGRAPHY.

Spaide RF.

From the Vitreous-Retina-Macula Consultants of New York, New York, New York; and the LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Hospital, New York, New York.

PURPOSE: To develop a method of imaging the retina using wide-field fluorescein angiography and use this method to investigate the areas of perfusion abnormalities in patients treated with ranibizumab for central retinal vein occlusion.

METHODS: Cross-sectional analysis of patients recruited to a prospective study. Patients in a prospective study of ranibizumab for central retinal vein occlusion were imaged with wide-field angiography. Fluorescein angiograms taken with the Optos P200 Scanning Laser Ophthalmoscope were obtained of the posterior portion of the eye and of the periphery through ocular steering. Resultant images of the periphery were registered to the posterior image using thin-plate spline warping. A transformation was used to measure the retinal surface area. Perfusion characteristics were compared with injection frequencies and protocol refraction visual acuity measurements.

RESULTS: Of 22 patients imaged, 7 would be classified as nonperfused by the Central Retinal Vein Occlusion Study (CVOS) angiographic criteria. However, all patients showed confluent areas of nonperfusion in the retinal periphery ranging in size from 16 disk areas to 242 disk areas. The areas of peripheral nonperfusion were not significantly different in the Central Retinal Vein Occlusion Study-perfused group versus nonperfused group. The area of peripheral nonperfusion was not correlated with the number of injections ($r = -0.13$, $P = 0.58$), but was inversely correlated with visual acuity ($r = -0.52$, $P = 0.013$). Blood vessels at the border of the peripheral nonperfusion did not show signs of neovascular growth or profuse leakage.

CONCLUSION: Angiographic mapping of the retina is possible using image-processing techniques with wide-field images. Eyes with central retinal vein occlusion develop widespread peripheral vascular obliteration in regions that are difficult to image with conventional fundus cameras. These nonperfused areas may have important implications for visual function.

PMID: 21487338 [PubMed - as supplied by publisher]

Retina. 2011 Apr 9. [Epub ahead of print]

TREATMENT OF NON-AGE-RELATED MACULAR DEGENERATION SUBMACULAR DISEASES WITH MACULAR TRANSLOCATION SURGERY.

Ehlers JP, Maldonado R, Sarin N, Toth CA.

From the Duke Eye Center, Retina Service, Durham, North Carolina.

PURPOSE: To evaluate the use of macular translocation surgery 360 in blinding submacular diseases other than age-related macular degeneration.

METHODS: A retrospective, consecutive case review was performed of subjects treated with macular translocation surgery 360 for a submacular disease other than age-related macular degeneration. Primary outcome was change in visual acuity. Clinical data were collected and analyzed, including demographics, visual acuity, imaging features, surgery details, and complications.

RESULTS: The review identified 16 subjects who had undergone macular translocation surgery 360 from 1996 to 2009 for submacular diseases other than age-related macular degeneration. These diseases included Best disease (n = 2), angioid streaks (n = 1), pathologic myopia (n = 3), punctate inner choroidopathy (n = 2), presumed ocular histoplasmosis syndrome (n = 3), central serous chorioretinopathy (n = 1), adult-onset vitelliform macular dystrophy (n = 3), and North Carolina macular dystrophy (n = 1). Mean preop visual acuity was 20/135 (range, 20/50-20/500). A ≤3-line acuity loss was seen in 13 of 16 (81%) subjects. Mean postop visual acuity was 20/110 (range, 20/40-20/1,000). The most common postop complications included epiretinal membrane (50%), cystoid macular edema (31%), residual diplopia (25%), retinal detachment (13%), and recurrent choroidal neovascularization (13%). Mean follow-up was 28 months (range, 4-61 months).

CONCLUSION: Macular translocation surgery 360 may be considered in subjects with progressive bilateral vision loss from various conditions other than age-related macular degeneration. Although a significant number of complications occurred, a large percentage of subjects gained >3 lines of visual acuity (38%) and achieved a final visual acuity of ≥20/50 (31%).

PMID: 21487342 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Apr 11. [Epub ahead of print]

Reproducibility of segmentation error correction in age-related macular degeneration: Stratus versus Cirrus OCT.

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

Vienna, Austria.

Introduction: The accuracy of retinal thickness measurement in age-related macular degeneration by optical coherence tomography (OCT) is affected by threshold algorithm line errors. The reproducibility of error correction in Stratus and Cirrus OCT should be examined.

Methods: OCT examinations of a consecutive series of 104 patients with neovascular age-related macular degeneration included in another study were reviewed. 72 eyes exhibited failures in Stratus OCT and 32 eyes in Cirrus OCT and were included in this new study. Algorithm line failures of Stratus OCT (retinal thickness program) and Cirrus OCT (Macular Cube 512×128 program) were corrected independently twice by two ophthalmologists and two residents, respectively, using the Stratus and Cirrus OCT built-in software. Reproducibility was assessed by the interclass correlation coefficient (ICC).

Results: The corrected values of central retinal thickness were significantly lower than the automated measured values in Stratus OCT for all examiners ($p<0.001$), while in Cirrus OCT the differences were not significant ($p=0.06$-0.09). For Stratus OCT, the ICC for central retinal thickness was 0.991 and 0.997 for the experienced ophthalmologists and 0.89 and 0.97 for the residents. For Cirrus OCT, the ICC was 1.0 and 1.0 for the experienced ophthalmologists and 0.99 and 0.95 for the residents.

Conclusion: The reproducibility of threshold algorithm line failure correction was good overall in Stratus and Cirrus OCT and can therefore be recommended to improve retinal thickness measurement, particularly when experienced examiners perform the corrections.

PMID: 21486740 [PubMed - as supplied by publisher]

Epidemiology & pathogenesis

Curr Cancer Drug Targets. 2011 Apr 13. [Epub ahead of print]

VEGF/VEGFR Pathway Inhibitors as Anti-Angiogenic Agents: Present and Future.

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Abstract

Angiogenesis, the formation of new blood vessels from pre-existing ones, plays a central role in the process of tumor growth and metastasis. The proliferation of endothelium and formation of new blood vessels further the size of solid tumors. It is expected that blocking angiogenesis will be an efficient therapeutic approach against many tumor types. The key signaling system that regulates proliferation and migration of endothelial cells are vascular endothelium growth factor (VEGF) and their receptors (VEGFR-1, -2 and -3). VEGFR-2, a receptor with higher affinity and greater kinase activity, is more important in the direct regulation of angiogenesis, mitogenic signaling, and permeability-enhancing effects. VEGFRs are expressed at high levels in many types of human solid tumors, including glioma, lung, breast, renal, ovarian and gastrointestinal tract carcinomas. Inhibition of VEGFR has emerged as a potential therapy method for cancers and it has been clinically validated with FDA-approvals of bevacizumab, sorafenib, and suntinib. Consequently, a number of small molecules with VEGFR inhibitory properties have been developed. Many of these have been evaluated as potent inhibitors and some are currently in clinical-trials for various angiogenic related disorders including inflammatory diseases, retinopathies and age related macular degeneration. This review reports various VEGF/VEGFR pathway inhibitors such as small molecules and monoclonal antibodies, along with their reported activities.

PMID: 21486218 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Apr 11. [Epub ahead of print]

Sustainability of visual acuity in the first 2 years after cataract surgery.

Fong CS, Mitchell P, Rochtchina E, de Loryn T, Hong T, Wang JJ.

Department of Ophthalmology, Westmead Millennium Institute, University of Sydney, Sydney, Australia.

Purpose: To assess whether improved visual acuity (VA) is sustained 2 years after the cataract surgery.

Methods: The Cataract Surgery and Age-Related Macular Degeneration (CSAMD) study followed 1936 patients aged ≥65 years undergoing phacoemulsification cataract surgery at Westmead Hospital (Sydney, Australia) between 2004 and 2007. Presenting and pinhole VA were assessed and retinal photography was performed annually. VA improvement or reduction was defined if VA differed by ≥2 lines between 1 and 24 months.

Results: VA data were available for 1809 patients at 1 month and 1294 at both postoperative visits (71.5% of 1809). At the 2-year visit, 930 patients (71.9%) maintained the same pinhole VA levels that they had at 1 month postoperatively, 199 (15.4%) had an improvement and 165 (12.7%) a reduction in pinhole VA. After adjusting for age and gender, pre-existing macular conditions (early AMD, macular hole or previous laser treatment) were associated with pinhole VA reduction (p=0.02). At the 24-month visit, 58.1% of those with presenting VA improvement wore distance spectacles.

Conclusions: One in eight cataract surgical patients lost at least two lines in pinhole VA over the 2-year postoperative period. Regular eye examinations of patients after cataract surgery may help to maximise the surgical benefits over the long term.

PMID: 21486741 [PubMed - as supplied by publisher]

Stem Cells. 2011 Mar 24. doi: 10.1002/stem.635. [Epub ahead of print]

Human iPS-Derived Retinal Pigment Epithelium (RPE) Cells Exhibit Ion Transport, Membrane Potential, Polarized VEGF Secretion and Gene Expression Pattern Similar to Native RPE.

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Abstract

Aged-related macular degeneration (AMD) is one of the major causes of blindness in aging population and progresses with death of retinal pigment epithelium (RPE) and photoreceptor degeneration inducing impairment of central vision. Discovery of human induced pluripotent stem (hiPS) cells has opened new avenues for the treatment of degenerative diseases using patient specific stem cells to generate tissues and cells for autologous cell-based therapy. Recently, RPE cells were generated from hiPS cells. However, there is no evidence that those hiPS-derived RPE possess specific RPE functions that fully distinguish them from other type of cells. Here we show for the first time that RPE generated from hiPS under defined conditions exhibit ion transport, membrane potential, polarized VEGF secretion and gene expression profile similar to those of native RPE. The hiPS-RPE could therefore be a very good candidate for RPE replacement therapy in AMD. However, these cells show rapid telomere shortening, DNA chromosomal damage and increased p21 expression that cause cell growth arrest. This rapid senescence might affect the survival of the transplanted cells in vivo and therefore, only the very early passages should be used for regeneration therapies. Future research needs to focus on the generation of "safe" as well as viable hiPS-derived somatic cells.

PMID: 21480547 [PubMed - as supplied by publisher]

Pre-clinical

Lik Sprava. 2010 Jul-Sep;(5-6):21-30.

[Use of nanotechnology and nanomaterials in ophthalmology].

[Article in Ukrainian]

[No authors listed]

Abstract

Peculiarities of anatomy, histology and physiology of eyes, do not allow to create an effective concentration of a medication in damaged tissues by traditional methods. Therefore, effective remedy delivery to a pathological focus is an current issue for ophthalmologists, pharmacologists and pharmacists. One of the perspective ways to solve this problem is nanotechnology. The use of nanomaterials (nanoparticles, dendrimers, cyclodextrins, liposomes, niosomes, diskomes), medicine formulations (microemulsions, hydrogel systems, nanosuspenisons) and ways of medicine delivery and nanomaterials (contact lenses, microneedles, intraocular implants, iontophoresis), open new possibilities in the treatment of serious eye diseases, such as glaucoma, diabetic retinopathy, macular degeneration, uveitises of different etiology. It will establish new high level therapy standards in ophthalmology in future. Aspects of possible complications and long-term effects of application of these technologies are still poorly explored and need further development and improvement. Despite of it, this new direction of the treatment in ophthalmology is very important and perspective.

PMID: 21488365 [PubMed - in process]

Diet

Biofactors. 2011 Mar;37(2):104-16. doi: 10.1002/biof.152.

Post-translational protein modification by carotenoid cleavage products.

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Abstract

Carotenoids are known to generate various aldehydes, known as carotenoid-derived aldehydes (CDAs), which could efficiently react with protein or DNA. In this in vitro model study, interaction between CDA and protein has been studied. Various proteins were incubated with CDA, and protein modification and adduct formation were confirmed by using matrix-assisted laser desorption and ionization time-of-flight, amino acid analysis, and measuring enzyme activity on modification with CDA. Using radiolabeled NaB((3) H)H(4) and Raney nickel as well as sulfhydryl assay (Ellman's reagent), we confirmed that CDA could conjugate with cysteine through a thioether linkage. The carbonyl assay using 2,4-dinitrophenylhydrazine revealed the possible involvement of Schiff's base reaction between CDA and lysine. The adducts formed between β-apo-8-carotenal (BA8C) and N-acetylcysteine and BA8C and N-acetyllysine were confirmed by HPLC and ESI-MS. Our results suggest that CDA could alter protein function by post-translational interaction with cysteine and lysine by thioether linkage and by schiff's based bonds, respectively. Thus, the formation of CDA adducts with proteins could alter functional properties of proteins responsible for maintaining cell homeostasis and thereby cause cellular toxicity. In view of these observations, further studies are required to understand the delicate balance between beneficial and/or harmful effects of carotenoids as a dietary supplement to slow age-related macular degeneration progression.

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Vitamin D Status and Early Age-Related Macular Degeneration in Postmenopausal Women.

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OBJECTIVE: The relationship between serum 25-hydroxyvitamin D (25[OH]D) concentrations (nmol/L) and the prevalence of early age-related macular degeneration (AMD) was investigated in participants of the Carotenoids in Age-Related Eye Disease Study.

METHODS: Stereoscopic fundus photographs, taken from 2001 to 2004, assessed AMD status. Baseline (1994-1998) serum samples were available for 25(OH)D assays in 1313 women with complete ocular and risk factor data. Odds ratios (ORs) and 95% confidence intervals (CIs) for early AMD (n = 241) of 1287 without advanced disease were estimated with logistic regression and adjusted for age, smoking, iris pigmentation, family history of AMD, cardiovascular disease, diabetes, and hormone therapy use.

RESULTS: In multivariate models, no significant relationship was observed between early AMD and 25 (OH)D (OR for quintile 5 vs 1, 0.79; 95% CI, 0.50-1.24; P for trend = .47). A significant age interaction (P = .002) suggested selective mortality bias in women aged 75 years and older: serum 25(OH)D was associated with decreased odds of early AMD in women younger than 75 years (n = 968) and increased odds in women aged 75 years or older (n = 319) (OR for quintile 5 vs 1, 0.52; 95% CI, 0.29-0.91; P for trend

= .02 and OR, 1.76; 95% CI, 0.77-4.13; P for trend = .05, respectively). Further adjustment for body mass index and recreational physical activity, predictors of 25(OH)D, attenuated the observed association in women younger than 75 years. Additionally, among women younger than 75 years, intake of vitamin D from foods and supplements was related to decreased odds of early AMD in multivariate models; no relationship was observed with self-reported time spent in direct sunlight.

CONCLUSIONS: High serum 25(OH)D concentrations may protect against early AMD in women younger than 75 years.

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