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Drug treatment

Retina. 2011 Dec 5. [Epub ahead of print]

EFFECT OF INTRAVITREAL BEVACIZUMAB ON RETROBULBAR BLOOD FLOW IN INJECTED AND UNINJECTED FELLOW EYES OF PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

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BACKGROUND: To determine the effect of intravitreal administration of bevacizumab (1.25 mg/0.05 mL) on retrobulbar circulation of the injected and the fellow (uninjected) eyes in patients with neovascular age-related macular degeneration.

METHODS: In this prospective study, the retrobulbar hemodynamics of 43 patients with neovascular age-related macular degeneration was examined by color Doppler ultrasonography. Peak systolic velocity, end-diastolic velocity, and resistive index values in the central retinal artery and short posterior ciliary artery in both injected and uninjected fellow eyes were measured at baseline and 7 days after a single intravitreal injection of bevacizumab.

RESULTS: At baseline, the peak systolic velocity, end-diastolic velocity, and the resistive index in the central retinal artery and short posterior ciliary artery of the injected eye were not significantly different compared with the fellow uninjected eye ($P > 0.05$ for all). However, intravitreal bevacizumab induced a significant reduction in the peak systolic velocity and end-diastolic velocity and a significant rise in the resistive index of the central retinal artery and short posterior ciliary artery of the injected eye ($P \leq 0.006$ for all). Peak systolic velocity and end-diastolic velocity decreased in the central retinal artery ($P = 0.023$ and $P = 0.030$) and the short posterior ciliary artery ($P = 0.001$ and $P < 0.000$) in the uninjected eye while the resistive index did not significantly change in central retinal artery ($P = 0.114$) and short posterior ciliary artery ($P = 0.082$) of the fellow eyes.

CONCLUSION: Intravitreal injection of bevacizumab significantly affects ocular hemodynamic parameters of both the injected and the uninjected fellow eyes with neovascular age-related macular degeneration.

PMID: 22146127 [PubMed - as supplied by publisher]

Ophthalmology. 2011 Dec;118(12):e5-e14.

Rationale for the diabetic retinopathy clinical research network treatment protocol for center-involved diabetic macular edema.

Diabetic Retinopathy Clinical Research Network; Writing Committee, Aiello LP, Beck RW, Bressler NM, Browning DJ, Chalam KV, Davis M, Ferris FL 3rd, Glassman AR, Maturi RK, Stockdale CR, Topping TM.

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OBJECTIVE: To describe the underlying principles used to develop a web-based algorithm that incorporated intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment for diabetic macular edema (DME) in a Diabetic Retinopathy Clinical Research Network (DRCR.net) randomized clinical trial.

DESIGN: Discussion of treatment protocol for DME.

PARTICIPANTS: Subjects with vision loss resulting from DME involving the center of the macula.

METHODS: The DRCR.net created an algorithm incorporating anti-VEGF injections in a comparative effectiveness randomized clinical trial evaluating intravitreal ranibizumab with prompt or deferred (≥ 24 weeks) focal/grid laser treatment in eyes with vision loss resulting from center-involved DME. Results confirmed that intravitreal ranibizumab with prompt or deferred laser provides superior visual acuity outcomes compared with prompt laser alone through at least 2 years. Duplication of this algorithm may not be practical for clinical practice. To share their opinion on how ophthalmologists might emulate the study protocol, participating DRCR.net investigators developed guidelines based on the algorithm's underlying rationale.

MAIN OUTCOME MEASURES: Clinical guidelines based on a DRCR.net protocol.

RESULTS: The treatment protocol required real-time feedback from a web-based data entry system for intravitreal injections, focal/grid laser treatment, and follow-up intervals. Guidance from this system indicated whether treatment was required or given at investigator discretion and when follow-up should be scheduled. Clinical treatment guidelines, based on the underlying clinical rationale of the DRCR.net protocol, include repeating treatment monthly as long as there is improvement in edema compared with the previous month or until the retina is no longer thickened. If thickening recurs or worsens after discontinuing treatment, treatment is resumed.

CONCLUSIONS: Duplication of the approach used in the DRCR.net randomized clinical trial to treat DME involving the center of the macula with intravitreal ranibizumab may not be practical in clinical practice, but likely can be emulated based on an understanding of the underlying rationale for the study protocol. Inherent differences between a web-based treatment algorithm and a clinical approach may lead to differences in outcomes that are impossible to predict. The closer the clinical approach is to the algorithm used in the study, the more likely the outcomes will be similar to those published.

PMID: 22136692 [PubMed - in process]

Other treatment & diagnosis

Eur J Ophthalmol. 2011 Nov 28:0. doi: 10.5301/ejo.5000087. [Epub ahead of print]

Reproducibility of fluorescein and indocyanine green angiographic assessment for RAP diagnosis: a multicenter study.

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Purpose: To explore the interobserver agreement in the diagnosis of retinal angiomatous proliferation (RAP) using fluorescein (FA) and indocyanine green angiographies (ICGA) and to detect which morphologic features of the neovascular lesion are associated with RAP diagnosis.

Methods: In this cross-sectional study, consecutive patients with newly diagnosed neovascular age-related macular degeneration (AMD) evaluated in 8 retina centers were considered. The FA and ICGA were obtained in all centers according to a standard protocol, both performed either as a static or as a dynamic examination. All images were graded by 2 observers from different institutions.

Results: A total of 201 eyes with neovascular AMD of 155 consecutive patients (mean age 76 ± 8 years) were considered. Overall RAP prevalence was 30% using FA and 26% using ICGA. Patients studied with dynamic angiography were twice as likely to be diagnosed with RAP as those using static angiography. Interobserver agreement for the overall detection of RAP was high using FA (kappa: 0.868; 95% confidence interval [CI]: 0.793-0.944) and very high using ICGA (kappa: 0.905; 95% CI 0.836-0.974). The agreement between the 2 observers tended to be higher for the truncated vessel than for the anastomosis in FA as well as in ICGA, but no comparison yielded statistical significance ($p=0.258$ and $p=0.584$, respectively).

Conclusions: The interobserver agreement for RAP detection was very good both using FA and ICGA, but the overall detection of RAP was higher for dynamic strategy compared with static one.

PMID: 22139618 [PubMed - as supplied by publisher]

J Vis. 2011 Dec 5;11(14). pii: 4. doi: 10.1167/11.14.4. Print 2011.

Decoding simulated neurodynamics predicts the perceptual consequences of age-related macular degeneration.

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Abstract

Age-related macular degeneration (AMD) is the major cause of blindness in the developed world. Though substantial work has been done to characterize the disease, it is difficult to predict how the state of an individual's retina will ultimately affect their high-level perceptual function. In this paper, we describe an approach that couples retinal imaging with computational neural modeling of early visual processing to generate quantitative predictions of an individual's visual perception. Using a patient population with mild to moderate AMD, we show that we are able to accurately predict subject-specific psychometric performance by decoding simulated neurodynamics that are a function of scotomas derived from an individual's fundus image. On the population level, we find that our approach maps the disease on the retina to a representation that is a substantially better predictor of high-level perceptual performance than traditional clinical metrics such as drusen density and coverage. In summary, our work identifies possible new metrics for evaluating the efficacy of treatments for AMD at the level of the expected changes in high-level visual perception and, in general, typifies how computational neural models can be used as a framework to characterize the perceptual consequences of early visual pathologies.

PMID: 22144563 [PubMed - in process]

Pathogenesis

Graefes Arch Clin Exp Ophthalmol. 2011 Dec 3. [Epub ahead of print]

The effect of connexin43 on the level of vascular endothelial growth factor in human retinal pigment epithelial cells.

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BACKGROUND: Connexins (Cx) are the basic units of gap junctions and contribute to cellular integrity by promoting intercellular communication. Disruption of the retinal pigment epithelial monolayer may be an early event in the pathogenesis of age-related macular degeneration, a condition in which vascular endothelial growth factor (VEGF) is known to be of importance. This study was designed to assess the effect of connexin43 (Cx43) expression and gap junctional intercellular communication (GJIC) on the expression and secretion of VEGF from the retinal pigment epithelium under normal cell culture and oxidative stress conditions.

METHODS: Stable cell lines of ARPE-19 were produced in which wild-type Cx43 was either over-expressed, down-regulated by targeted shRNA, or functionally inhibited by co-expression of a disease-linked dominant-negative mutant (G21R). Pharmacologic blockade of GJIC was accomplished with flufenamic acid. Oxidant challenge was performed with tert-butyl hydroperoxide (tBH). VEGF gene expression and secretion were assessed by real-time PCR and ELISA respectively.

RESULTS: Over-expression of Cx43 in ARPE-19 cells reduced both gene expression and secretion of VEGF. Down-regulation of Cx43 increased gene expression and secretion of VEGF. Increased secretion of VEGF was also observed in ARPE-19 cells expressing a dominant-negative mutant of Cx43, and when GJIC was blocked. Over-expression of Cx43 reduced tBH-induced secretion of VEGF from ARPE-19 cells.

CONCLUSIONS: These studies show that Cx43 protects against oxidative stress-induced VEGF secretion in ARPE-19 cells, and thus has important implications in understanding the pathogenesis of age-related macular degeneration.

PMID: 22138732 [PubMed - as supplied by publisher]

Epidemiology

Surv Ophthalmol. 2011 Nov 30. [Epub ahead of print]

Causes of Blindness and Visual Impairment in Latin America.

Furtado JM, Lansingh VC, Carter MJ, Milanese MF, Peña BN, Gherzi HA, Bote PL, Nano ME, Silva JC.

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Abstract

We review what is known in each country of the Latin American region with regards to blindness and visual impairment and make some comparisons to Hispanic populations in the United States. Prevalence of blindness varied from 1.1% in Argentina to 4.1% in Guatemala in people 50 years of age and older, with the major cause being cataract. Diabetic retinopathy and glaucoma are starting to make serious inroads, although epidemiological data are limited, and age-related macular degeneration is now a concern in some populations. Infectious diseases such as trachoma and onchocerciasis are quickly diminishing. Although progress has been made, retinopathy of prematurity remains the major cause of childhood blindness. If

VISION 2020 is to succeed, many more epidemiological studies will be needed to set priorities, although some can be of the Rapid Assessment of Avoidable Blindness design. Developing the infrastructure for screening and treatment of ophthalmic disease in Latin America continues to be a challenge.

PMID: 22137039 [PubMed - as supplied by publisher]

Diet

Drugs. 2011 Dec 24;71(18):2421-34. doi: 10.2165/11596840-000000000-00000.

Use of herbal medicines and nutritional supplements in ocular disorders: an evidence-based review.

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Abstract

We sought to examine the evidence regarding the use of herbal medicines and nutritional supplements in age-related macular degeneration (AMD), cataracts, diabetic retinopathy and glaucoma, and to review the ocular adverse effects of herbal and nutritional agents of clinical importance to ophthalmologists. We performed a literature search of Ovid MEDLINE and selected websites including the American Academy of Ophthalmology (AAO), the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH) and the World Health Organization (WHO). There is strong evidence supporting the use of antioxidants and zinc in patients with certain forms of intermediate and advanced AMD. However, there has been growing evidence regarding potential significant adverse effects associated with the AREDS (Age-Related Eye Disease Study) formula vitamins. Current data does not support the use of antioxidants or herbal medications in the prevention or treatment of cataracts, glaucoma or diabetic retinopathy. It is important for providers to be aware of the benefits and the significant potential adverse effects that have been associated with nutritional supplements and herbal medications, and to properly inform their patients when making decisions about supplementation. Further rigorous evaluation of nutritional supplements and herbal medicines in the treatment of eye disease is needed to determine their safety and efficacy.

PMID: 22141385 [PubMed - in process]

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