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MD Research News

Issue 245

Tuesday 25 August, 2015

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Drug treatment

Curr Med Res Opin. 2015 Aug 21:1-30. [Epub ahead of print]

Ranibizumab vs. aflibercept for wet age-related macular degeneration: Network meta-analysis to understand the value of reduced frequency dosing.

Szabo SM, Hedegaard M, Chan K, Thorlund K, Christensen R, Vorum H, Jansen JP.

OBJECTIVE: Although a reduced aflibercept (2.0mg) injection frequency relative to the approved dosing posology is included in national treatment guidelines for wet age-related macular degeneration (AMD), there is limited evidence of its comparative efficacy. The objective was to compare the efficacy and safety of reduced frequency dosing for aflibercept, relative to other approved and marketed vascular endothelial growth factor inhibitors for wet AMD, over 12 months.

RESEARCH DESIGN AND METHODS: Based on a systematic literature review performed according to a pre-specified protocol, a Bayesian network meta-analysis (NMA) was conducted to indirectly compare posologies of aflibercept and ranibizumab (0.5mg). The efficacy outcome, mean change from baseline in best-corrected visual acuity (BCVA) on the ETDRS chart, was evaluated at 3 and 12 months; and safety data at 12 months. Standard NMA models were used to analyze change at 3 months, and fractional polynomial regression over 12 months. Safety data were analyzed using binomial models with a logistic link function.

RESULTS: Five trials formed a complete evidence network. At three months, all posologies of aflibercept and ranibizumab resulted in similar changes in BCVA. Over 12 months, approved posologies of aflibercept and ranibizumab resulted in similar changes from baseline (between 6.7 (95% credible interval [CrI], 5.5, 7.8) to 9.1 (8.1, 10.1) ETDRS letters); however, reduced frequency aflibercept was associated with a smaller change (1.8 letters, [-25.9, 29.2]). There was a trend towards a greater change in BCVA, with increasing frequency of dosing. All posologies performed similarly with respect to safety, and CrIs were wide.

CONCLUSIONS: Approved posologies of ranibizumab and aflibercept are similarly effective treatments for wet AMD. Reduced frequency aflibercept was associated with the poorest visual outcomes, and sample sizes were small. Findings from these analyses provide novel evidence of the comparative efficacy and safety of aflibercept and ranibizumab for wet AMD.

PMID: 26296050 [PubMed - as supplied by publisher]

J Ophthalmol. 2015;2015:324841. Epub 2015 Jul 29.

Ranibizumab for Visual Impairment due to Diabetic Macular Edema: Real-World Evidence in the Italian Population (PRIDE Study).

Menchini U, Bandello F, De Angelis V, Ricci F, Bonavia L, Viola F, Muscianisi E, Nicolò M.

Purpose: An expanded access program (PRIDE study) in Italy to provide ranibizumab 0.5 mg to diabetic macular edema (DME) patients, prior to reimbursement.

Methods: Open-label, prospective, phase IIIb study. Majority of patients were not treatment-naïve before enrollment. Patients received ranibizumab as per the EU label (2011). Safety was assessed by incidences of ocular/systemic adverse events (AEs) and serious AEs (SAEs) and efficacy in terms of visual acuity (VA) change from baseline (decimal score or Snellen (20/value)).

Results: Overall, 515 patients (83.5%) completed the study. In unilateral/bilateral patients, commonly observed AEs were cardiac disorders (1.3%/1.3%) and nervous system disorders (1.3%/1.1%); SAEs were reported in 4.5%/4.8% of patients. Acute renal failure, lung carcinoma, and cardiac arrest were the causes of death in one unilateral and two bilateral patients. Ranibizumab improved/maintained VA (Snellen (20/value)/decimal scores) in both unilateral (up to -16.7/1.5) and bilateral patients (up to -23.6/1.2) at Month 5, with a mean of 4.15 and 4.40 injections, respectively. Overall, no difference was observed in the VA outcomes and treatment exposure between unilateral/bilateral patients.

Conclusions: The PRIDE study provided early ranibizumab access to >600 Italian patients. Ranibizumab was well-tolerated and improved/maintained VA in 40.2%-68.8% patients, with no differences in case of unilateral or bilateral pathology. The study is registered with EudraCT.

PMID: 26294963 [PubMed] PMCID: PMC4532943

Curr Diab Rep. 2015 Oct;15(10):652.

Novel Therapies in Development for Diabetic Macular Edema.

Agarwal A, Afridi R, Hassan M, Sadiq MA, Sepah YJ, Do DV, Nguyen QD.

Abstract: Diabetic macular edema (DME) secondary to diabetic retinopathy (DR) is a major cause for functional visual loss in the developed world. Laser photocoagulation has been used for decades in the treatment of DME. However, the advent of anti-vascular endothelial growth factor (anti-VEGF) has revolutionized the treatment of DME. Three important anti-VEGF agents whose efficacy has been well established via phase III clinical trials include ranibizumab, bevacizumab, and aflibercept. However, even in the era of anti-VEGF therapies, there are some challenges that retina specialists have to confront in managing patients with DME. These include the need for frequent treatment and an unpredictable response to therapy. There is evidence to suggest that pathways other than the VEGF pathway may be playing a role in the development of DME. Thus, extensive research is focused on development of novel agents that target these pathways. This review focuses on novel therapeutic agents in development, which may be used as a monotherapy or in combination with anti-VEGF agents, for the management of DME in the future.

PMID: 26294336 [PubMed - in process]

BMC Ophthalmol. 2015 Aug 20;15:109.

Comparison of Eylea® with Lucentis® as first-line therapy in patients with treatment-naïve neovascular age-related macular degeneration in real-life clinical practice: retrospective case-series analysis.

Böhni SC, Bittner M, Howell JP, Bachmann LM, Faes L, Schmid MK.

BACKGROUND: To identify differences between Ranibizumab and Aflibercept in treatment-naïve patients with neovascular age-related macular degeneration (nvAMD) in a real-life clinical setting.

METHODS: We compared two groups of patients with a fairly similar prognosis either receiving Aflibercept

or Ranibizumab within a pro re nata regimen for 1 year. Changes in visual acuity (letters) and central foveal thickness (CFT) and frequency of injections after completing the loading phase were evaluated using two separate multivariate mixed linear models.

RESULTS: When correcting for baseline differences between the Aflibercept (11 eyes) and Ranibizumab (16 eyes) group, there was neither divergence in visual acuity (-0.97 letters (95 % CI. -6.06-4.12); p = 0.709), nor a significant difference in the reduction of CFT (-25.16 µm, 95 % CI; (-78.01-27.68); p = 0.351) between the two groups 1 year after treatment initiation. Also, the number of injection did not differ (0.04 (95 % CI; -0.16-0.09); p = 0.565).

CONCLUSION: In contrast to health claims, treatment-naïve nvAMD, Ranibizumab and Aflibercept were equivalent in terms of functional and morphologic outcomes and number of injections when studied in real-life clinical practice.

PMID: 26289356 [PubMed - in process] PMCID: PMC4546020

Expert Rev Clin Pharmacol. 2015 Sep;8(5):541-8. Epub 2015 Aug 10.

Conbercept (KH-902) for the treatment of neovascular age-related macular degeneration.

Nguyen TT, Guymer R.

Abstract: Age-related macular degeneration (AMD) is a progressive, degenerative disease of the retina that occurs with increasing incidence with age and ranks third among the global causes of visual impairment. VEGF has been implicated in the development and progression of neovascular AMD. Drugs that block VEGF, leading to regression of the abnormal blood vessels, are the mainstay of treatment of neovascular AMD, particularly for subfoveal neovascular lesions. Anti-VEGF agents currently in use in neovascular AMD are pegaptanib (Macugen(®)), ranibizumab (Lucentis(®)), bevacizumab (Avastin(®)) and a soluble VEGF receptor decoy aflibercept (Eylea(®)). Recently, China Food and Drug Administration have approved conbercept for the treatment of neovascular AMD in China. Conbercept appears to offer yet another anti-VEGF drug for use in neovascular AMD. However, there is still a need for large, well-designed, randomized clinical trials to ensure its safety and efficacy.

PMID: 26289225 [PubMed - in process]

Retin Cases Brief Rep. 2015 Aug 17. [Epub ahead of print]

SUBRETINAL NEOVASCULARIZATION IN MACULAR TELANGIECTASIA TYPE 2: OPTICAL COHERENCE TOMOGRAPHIC ANGIOGRAPHY AND TREATMENT RESPONSE.

Tan GS, Kuehlewein L, Sadda SR, Sarraf D, Schwartz SD.

PURPOSE: To report the optical coherence tomographic angiography findings and response to treatment in a case of macular telangiectasia Type 2 with subretinal neovascularization.

METHODS: Case report.

RESULTS: A 64-year-old man with macular telangiectasia Type 2 developed subretinal neovascularization, which was imaged on optical coherence tomographic angiography. He was treated with intravitreal aflibercept, and there was a remarkable reduction of flow in the subretinal neovascular network on optical coherence tomographic angiography.

CONCLUSION: Optical coherence tomographic angiography provides detailed information on the retinal microvasculature and subretinal neovascularization in macular telangiectasia Type 2. It can be used to assess response to treatment.

PMID: 26288110 [PubMed - as supplied by publisher]

Neoplasma. 2015 Aug 19. [Epub ahead of print]

Minireview on current antiangiogenic agents in oncology and ophthalmology.

Cernak M, Nogova L.

Abstract: Antiangiogenic drugs are approved for many cancer types for longer than a decade. Furthermore, several antiangiogenic agents are approved for local application in ophthalmology for treatment of macular degeneration, venous retinal occlusion and diabetic retinopathy. Knowing that antiangiogenic agents are active in ocular system, we reviewed the current literature, whether antiangiogenic drugs may cause ocular side effects in cancer patients by systemic application. Furthermore, we searched in published papers, if systemic application of antiangiogenic agents in cancer patients may simultaneously treat their ocular disorders, if they have such. Finally, we emphasized cooperation between an oncologist and ophthalmologist when treating patients with antiangiogenic drugs.

PMID: 26286389 [PubMed - as supplied by publisher]

BMC Res Notes. 2015 Aug 19;8:358.

Macular hole formation following intravitreal injection of ranibizumab for branch retinal vein occlusion: a case report.

Muramatsu D, Mitsuhashi R, Iwasaki T, Goto H, Miura M.

BACKGROUND: Macular hole formation after anti-vascular endothelial growth factor therapy is a rare complication. We report macular hole formation after intravitreal ranibizumab injection for branch retinal vein occlusion.

CASE PRESENTATION: A 63-year-old Asian male was treated with intravitreal ranibizumab injection for chronic macular edema with branch retinal vein occlusion in his right eye. Before treatment, best-corrected visual acuity in his right eye was 20/200. Nine days after injection, a full thickness macular hole developed with reduction of macular edema. After pars plana vitrectomy combined with cataract surgery, the macular hole was successfully closed, and the best-corrected visual acuity in his right eye improved to 20/40.

CONCLUSION: The possibility of an infrequent complication like macular hole should be considered for intravitreal ranibizumab for macular edema with branch retinal vein occlusion.

PMID: 26285577 [PubMed - in process] PMCID: PMC4541740

Acta Ophthalmol. 2015 Aug 18. [Epub ahead of print]

The impact of ranibizumab on the level of intercellular adhesion molecule type 1 in the vitreous of eyes with proliferative diabetic retinopathy.

Yan Y, Zhu L, Hong L, Deng J, Song Y, Chen X.

PURPOSE: This study was to investigate the impact of ranibizumab on the level of intercellular adhesion molecule type 1 (ICAM-1) in the vitreous of eyes with PDR.

METHODS: This is an interventional case-control study. A total of 82 eyes from 82 patients who had undergone vitreous surgery for the treatment of retinal disorders were included. Twenty-two eyes with PDR received an intravitreal ranibizumab injection (IVR) 3-7 days before vitrectomy and were grouped as 'PDR with recent IVR' or Group 1. Sixteen eyes with PDR received IVR more than 7 days before vitrectomy and were grouped as 'PDR with remote IVR' or Group 2. Twenty-two matched PDR eyes did not receive IVR before vitrectomy and were grouped as 'PDR without IVR' or Group 3. Finally, 22 eyes from 22 patients with idiopathic macular pucker (IMP) served as the 'non-diabetic control' group, or Group 4. Vitreous samples were obtained at the time of vitrectomy from all eyes, and the levels of vascular endothelium growth factor

(VEGF) and ICAM-1 were analysed using ELISA.

RESULTS: PDR without IVR (Group 3) had the highest vitreous VEGF concentration; the difference was significant compared with those in the PDR with recent IVR (Group 1), PDR with remote IVR (Group 2) and the non-diabetic control group (Group 4) ($p < 0.001$). Group 2 had a lower vitreous VEGF level than Group 1 ($p = 0.041$). Group 1 had the highest vitreous ICAM-1 levels ($p < 0.001$ versus. Groups 2, 3 and 4); Group 2 had a lower vitreous ICAM-1 level than Group 3 ($p = 0.028$).

CONCLUSION: The vitreous fluid level of ICAM-1 was significantly increased within 1 week of IVR administration, but markedly decreased after a week of administration in eyes with PDR. This suggests that leucostasis, vascular leakage and endothelial dysfunction may be amplified in the early days after IVR, but that a therapeutic effect of IVR in these processes may appear after 1 week of ranibizumab administration in eyes with PDR.

PMID: 26285163 [PubMed - as supplied by publisher]

PLoS One. 2015 Aug 21;10(8):e0136515.

Correction: Treatment Frequency and Dosing Interval of Ranibizumab and Aflibercept for Neovascular Age-Related Macular Degeneration in Routine Clinical Practice in the USA.

PLOS ONE Staff.

Abstract: [This corrects the article DOI: 10.1371/journal.pone.0133968.].

PMID: 26295570 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Klin Monbl Augenheilkd. 2015 Aug 17. [Epub ahead of print]

[Fundus Autofluorescence Imaging].[Article in German]

Schmitz-Valckenberg S.

Abstract: Fundus autofluorescence (FAF) imaging allows for non-invasive mapping of changes at the level of the retinal pigment epithelium/photoreceptor complex and of alterations of macular pigment distribution. This imaging method is based on the visualisation of intrinsic fluorophores and may be easily and rapidly used in routine patient care. Main applications include degenerative disorders of the outer retina such as age-related macular degeneration, hereditary and acquired retinal diseases. FAF imaging is particularly helpful for differential diagnosis, detection and extent of involved retinal areas, structural-functional correlations and monitoring of changes over time. Recent developments include - in addition to the original application of short wavelength light for excitation ("blue" FAF imaging) - the use of other wavelength ranges ("green" or "near-infrared" FAF imaging), widefield imaging for visualisation of peripheral retinal areas and quantitative FAF imaging.

PMID: 26280647 [PubMed - as supplied by publisher]

Ophthalmologe. 2015 Aug 21. [Epub ahead of print]

[Gene therapy as a treatment concept for inherited retinal diseases].[Article in German]

Bellingrath JS, Fischer MD.

BACKGROUND: Gene therapy for inherited retinal diseases (IRDs) is currently being validated in several

clinical trials and is becoming a promising therapeutic option for these previously incurable diseases.

OBJECTIVES: The aim of this review is to give an overview of the concept, the application and the challenges associated with gene therapy. In particular, the pertinence of gene therapy for IRDs will be highlighted along with ongoing clinical trials in the field.

MATERIAL AND METHODS: A systematic review of relevant entries on gene therapy and on gene therapy for IRDs, in particular in PubMed and ClinicalTrials.gov.

RESULTS: Gene therapy is emerging not only as a therapy for monogenetic retinal diseases but also for complex genetic diseases, such as neovascular age-related macular degeneration. The discovery of adeno -associated viral vectors (AAVs) has marked a great improvement for IRD gene therapy. All clinical studies since 2006 demonstrated the safety and initial efficacy; however, not all expectations based on very successful preclinical studies were met.

CONCLUSION: In future we can expect gene therapy to continue to become more clinically relevant. More than ever, it is now essential to generate precise characterizations of the natural disease progression of IRDs through observational or retrospective studies in order to guarantee a most effective study design.

PMID: 26293194 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2015 Aug 1;56(9):5424-30.

IL-18 Immunotherapy for Neovascular AMD: Tolerability and Efficacy in Nonhuman Primates.

Doyle SL, López FJ, Celkova L, Brennan K, Mulfaul K, Ozaki E, Kenna PF, Kurali E, Hudson N, Doggett T, Ferguson TA, Humphries P, Adamson P, Campbell M.

PURPOSE: Age-related macular degeneration is the most common form of central retinal blindness in the elderly. Of the two end stages of disease, neovascular AMD-although the minority form-is the most severe. Current therapies are highly successful at controlling progression of neovascular lesions; however, a significant number of patients remain refractory to treatment and the development of alternative and additive therapies to anti-VEGFs is essential.

METHODS: In order to address the translational potential of interleukin (IL)-18 for use in neovascular AMD, we initiated a nonhuman primate tolerability and efficacy study for the use of intravitreally (IVT) administered clinical grade human IL-18 (SB-485232). Cynomolgus monkeys were injected IVT with increasing doses of human IL-18 (two each at 1000, 3000, and 10,000 ng per eye). In tandem, 21 monkeys were administered nine laser burns in each eye prior to receiving IL-18 as an IVT injection at a range of doses. Fundus fluorescein angiography (FFA) was performed on days 8, 15, and 22 post injection and the development of neovascular lesions was assessed.

RESULTS: We show intravitreal, mature, recombinant human IL-18 is safe and can reduce choroidal neovascular lesion development in cynomolgus monkeys.

CONCLUSIONS: Based on our data comparing human IL-18 to current anti-VEGF-based therapy, clinical deployment of IL-18 for neovascular AMD has the potential to lead to a new adjuvant immunotherapy-based treatment for this severe form of central blindness.

PMID: 26284546 [PubMed - in process]

Pathogenesis

J Leukoc Biol. 2015 Aug 20. [Epub ahead of print]

Parainflammation, chronic inflammation, and age-related macular degeneration.

Chen M, Xu H.

Abstract: Inflammation is an adaptive response of the immune system to noxious insults to maintain homeostasis and restore functionality. The retina is considered an immune-privileged tissue as a result of its unique anatomic and physiologic properties. During aging, the retina suffers from a low-grade chronic oxidative insult, which sustains for decades and increases in level with advancing age. As a result, the retinal innate-immune system, particularly microglia and the complement system, undergoes low levels of activation (parainflammation). In many cases, this parainflammatory response can maintain homeostasis in the healthy aging eye. However, in patients with age-related macular degeneration, this parainflammatory response becomes dysregulated and contributes to macular damage. Factors contributing to the dysregulation of age-related retinal parainflammation include genetic predisposition, environmental risk factors, and old age. Dysregulated parainflammation (chronic inflammation) in age-related macular degeneration damages the blood retina barrier, resulting in the breach of retinal-immune privilege, leading to the development of retinal lesions. This review discusses the basic principles of retinal innate-immune responses to endogenous chronic insults in normal aging and in age-related macular degeneration and explores the difference between beneficial parainflammation and the detrimental chronic inflammation in the context of age-related macular degeneration.

PMID: 26292978 [PubMed - as supplied by publisher]

Methods Mol Biol. 2015;1332:3-23.

VEGF Splicing and the Role of VEGF Splice Variants: From Physiological-Pathological Conditions to Specific Pre-mRNA Splicing.

Guyot M, Pagès G.

Abstract: During this past decade, the vascular endothelial growth factor (VEGF) pathway has been extensively studied. VEGF is a paradigm of molecular regulation since its expression is controlled at all possible steps including transcription, mRNA stability, translation, and pre-mRNA splicing. The latter form of molecular regulation is probably the least studied. This field has been neglected; yet different forms of VEGF with different sizes and different physiological properties issued from alternative splicing have been described a long time ago. Recently a new level of complexity was added to the field of splicing of VEGF pre-mRNA. Whereas thousands of publications have described VEGF as a pro-angiogenic factor, an alternative splicing event generates specific anti-angiogenic forms of VEGF that only differ from the others by a modification in the last six amino acids of the protein. According to the scientists who discovered these isoforms, which are indistinguishable from the pro-angiogenic ones with pan VEGF antibodies, some of the literature on VEGF is at least inexact if not completely false. Moreover, the presence of anti-angiogenic forms of VEGF may explain the disappointing efficacy of anti-VEGF therapies on the overall survival of patients with different forms of cancers and with wet age-related macular degeneration. This review focuses on the existence of the different alternative splice variants of VEGF and the molecular mechanisms associated with their expression and function.

PMID: 26285742 [PubMed - in process]

Epidemiology

Clin Experiment Ophthalmol. 2015 Aug 18. [Epub ahead of print]

Longitudinal Andhra Pradesh Eye Disease Study (APEDS3): rationale, study design and research methodology.

Khanna RC, Murthy GV, Marmamula S, Mettla AL, Giridhar P, Banerjee S, Shekhar K, Chakrabarti S, Gilbert C, Rao GN; Andhra Pradesh Eye Disease Study Group.

PURPOSE: To describe the rationale, objectives, study design and procedures for the longitudinal Andhra Pradesh Eye Disease Study (APEDS).

DESIGN: Longitudinal cohort study

PARTICIPANTS: Surviving cohort from the rural component of APEDS

METHODS: During 1996-2000, Andhra Pradesh Eye Disease Survey (APEDS) was conducted in three rural (n = 7771) and one urban (n = 2522) areas (now called APEDS1). In 2009-10, a feasibility exercise (APEDS2) for a longitudinal study (APEDS3) was undertaken in the rural clusters only, as urban clusters no longer existed. In APEDS3, a detailed interview will be done to collect data on sociodemographic factors, ocular and systemic history, risk factors, visual function, knowledge of eye diseases and barriers to accessing services. All participants will also undergo a comprehensive eye examination including photography of lens, optic disc and retina, Optic Coherence Tomography of the posterior segment, anthropometry, blood pressure and frailty measures.

MAIN OUTCOME MEASURES: Estimates of the incidence of visual impairment (VI) and age related eye disease (lens opacities, glaucoma, age-related macular degeneration) and the progression of eye disease (lens opacities, myopia) and associated risk factors.

RESULT: Of the 7,771 respondents examined in rural areas in APEDS1, 5,447 (70.1%) participants were traced in APEDS2. These participants will be re-examined

CONCLUSION: APEDS3 will provide data on the incidence and progression of VI and major eye diseases and their associated risk factors in India. The study will provide further evidence to aid planning eye care services. PMID: 26283446 [PubMed - as supplied by publisher]

South Med J. 2015 Aug;108(8):502-6.

Age-Related Macular Degeneration and Coronary Artery Disease in a VA Population.

Thomas J, Mohammad S, Charnigo R, Baffi J, Abdel-Latif A, Ziada KM.

OBJECTIVES: Age-related macular degeneration (AMD) is the leading cause of blindness in the United States. Although AMD shares multiple risk factors with coronary artery disease (CAD), the association between AMD and CAD has not been established. The objective of our study was to demonstrate an association between the diagnosis of AMD and CAD and/or major cardiovascular risk factors.

METHODS: We performed a retrospective chart review of >13,000 patients at the Lexington Veterans Affairs Medical Center. Patients diagnosed as having AMD served as cases, and patients diagnosed with cataract and no AMD served as controls. We examined the prevalence of CAD and associated risk factors in both groups using univariate analysis followed by multivariate analyses to examine the association between AMD and CAD after adjusting for known common risk factors.

RESULTS: We identified 3950 patients with AMD and 9166 controls. Patients with AMD were on average 6 years older than controls ($P < 0.001$) and had a significantly higher prevalence of CAD (39% vs 34%) and hypertension (88% vs 83%) but lower incidence of diabetes mellitus and smoking. Estimated odds ratio relating CAD to AMD was 1.22 (95% confidence interval 1.13-1.32; $P < 0.001$). The association between CAD and AMD remained significant in multivariate analyses in older individuals (76 years and older). When we conducted a secondary analysis and matched the AMD and non-AMD groups based on age, the association between CAD and AMD remained significant (39.4% in the AMD group vs 36.6% in the non-AMD group; $P = 0.011$).

CONCLUSIONS: These findings support the existence of an association between CAD and AMD, particularly in older adult patients in the predominantly male Veterans Affairs population. Such an association between AMD and systemic vascular disease justifies the potential coscreening for these conditions.

PMID: 26280780 [PubMed - in process] PMCID: PMC4544738

South Med J. 2015 Aug;108(8):507-8.

Commentary on "Age-Related Macular Degeneration and Coronary Artery Disease in a VA Population".

Berry AW, Bishara M.

PMID: 26280781 [PubMed - in process]

Diet, lifestyle & low vision

Mol Aspects Med. 2015 Aug 14. [Epub ahead of print]

Dietary glycemia as a determinant of health and longevity.

Whitcomb EA, Chiu CJ, Taylor A.

Abstract: Extending healthful life is a millennia-old dream and objective. During the intervening centuries a multitude of concoctions and remedies have been offered, usually with few substantiated results. During the last century it was demonstrated that limiting caloric intake is associated with extended life in many mammals, albeit results remain to be clarified in humans (Colman et al., 2009; Mattison et al., 2012; McCay et al., 1935; McCay and Crowell, 1934; Walford and Crew, 1989; Walford, 1986; Weindruch, 1984, 1991, 1996). A myriad of modeling studies have revealed signaling pathways that are associated with life extension and the last two decades have seen an interest in the types of dietary carbohydrates that might confer health advantage, and possibly longevity. Loss of vision due to age-related cataracts or age-related macular degeneration is widely prevalent, affecting about 85% and 15% of the elderly respectively. With centenarians among the fastest growing segments of societies, and with loss of vision a very costly personal and societal burden, there is keen interest in extending vision - that is, delaying age-related macular degeneration and cataract - or diminishing risk for these debilities. Using extensive epidemiologic and nutritional information from the Nurses' Health Study and Age-Related Eye Disease Study (AREDS) we determined that measures of total carbohydrate, and even more so, glycemic index (GI), are associated with visual health (Chiu et al., 2011; Chiu et al., 2006b, 2007c, 2007b, 2007c; Weikel and Taylor, 2011; Weikel et al., 2012a). We also modeled this relationship in mice in order to elucidate etiologic relationships between dietary glycemia, visual health, and genetics (Rowan et al., 2014; Uchiki et al., 2012).

PMID: 26282832 [PubMed - as supplied by publisher]