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MD Research News

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Drug treatment

Eye (Lond). 2014 Nov 7. [Epub ahead of print]

Two-year outcome of an observe-and-plan regimen for neovascular age-related macular degeneration: how to alleviate the clinical burden with maintained functional results.

Gianniou C, Dirani A, Ferrini W, Marchionno L, Decugis D, Deli A, Ambresin A, Mantel I.

Purpose: The purpose of this study was to report the 2-year outcome of an individually tailored 'observe-and-plan' treatment regimen for neovascular age-related macular degeneration (nAMD), and to investigate its clinical value in terms of functional outcome. This regimen aimed to reduce the clinical burden (visits) by employing individually fixed injection intervals, based on the predictability of an individual's need for retreatment.

Methods: This prospective case series included 104 patients (115 eyes) with nAMD. Following three loading doses of ranibizumab, the disease recurrence interval was determined in monthly observation visits. Retreatment was applied in a series of three injections with individually fixed intervals (2 weeks shorter than the recurrence interval), combined with periodic adjustment of the intervals. The allowed injection intervals in treatment plans ranged from 1 to 3 months. If there was no recurrence at 3 months, the patient could change to monitoring alone.

Results: Mean visual acuity (VA) improved by 8.7, 9.7, and 9.2 letters at months 3, 12, and 24, respectively. The mean number of injections was 7.8 and 5.8 during years 1 and 2, respectively, whereas the mean number of ophthalmic examinations was 4.0 and 2.9, respectively. The mean treatment interval (after the loading doses) was 2.0 months during year 1, and 2.2 months during year 2.

Conclusion: The observe-and-plan regimen significantly improved and maintained VA over the course of 2 years. This favourable functional outcome was achieved with fewer clinic visits compared with other regimens. Therefore, this observe-and-plan regimen has the potential to alleviate the clinical burden of nAMD treatment.

PMID: 25359289 [PubMed - as supplied by publisher]

Case Rep Ophthalmol Med. 2014;2014:219792. Epub 2014 Oct 1.

Macular oedema in idiopathic macular telangiectasia type 1 responsive to aflibercept but not bevacizumab.

Shibeeb O, Vaze A, Gillies M, Gray T.

Abstract: We report a patient with macular oedema due to type 1 macular telangiectasia responding to intravitreal aflibercept injection. A 51-year-old man was diagnosed with type 1 idiopathic macular

telangiectasia (IMT) in the right eye. The macular oedema was refractory to initial treatment with intravitreal bevacizumab and argon laser photocoagulation. The patient was then treated with intravitreal aflibercept injections, following which the macular oedema was completely resolved and his vision was significantly improved. Intravitreal aflibercept injection appears to improve vision and reduce persistent macular oedema secondary to type 1 IMT and demonstrated promising anatomical and visual outcomes.

PMID: 25349755 [PubMed] PMCID: PMC4198777

Br J Ophthalmol. 2014 Oct 28. pii: bjophthalmol-2014-305802. [Epub ahead of print]

Simulation contact lenses for AMD health state utility values in NICE appraisals: a different reality.

Butt T, Crossland MD, West P, Orr SW, Rubin GS.

BACKGROUND/AIMS: The National Institute for Health and Care Excellence (NICE) has recommended the use of ranibizumab for neovascular age-related macular degeneration (AMD) and for diabetic macular oedema (DMO) as part of its health technology appraisal process. In the economic evaluations of both interventions, utility values were derived from members of the general public wearing contact lenses with a central opacity that was meant to simulate the blind spot experienced by many patients with advanced retinal disease. This paper tests the validity of the contact lens simulation, and finding it to be invalid, explores the impact on prior economic evaluations.

METHODS: Visual acuity, contrast sensitivity and visual fields were assessed with and without simulation lenses in five healthy subjects with normal vision.

RESULTS: We identified important differences between the contact lens simulation and vision loss experienced by patients with AMD. The contact lens simulator did not cause the central scotoma which is characteristic of late-stage AMD and which leads to severe difficulty with everyday activities such as reading or recognising faces and objects. The contact lens instead caused a reduction in retinal illumination experienced by the subjects as a general dimming across the retina.

CONCLUSIONS: A contact lens with a central opacity does not simulate a central scotoma. The clinical differences between simulated and actual AMD suggest there has been an underestimation of the severity of AMD health states. This brings into question the validity of the economic evaluations of treatments for AMD and DMO used by NICE.

PMID: 25351679 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2014 Oct 18;7(5):855-9. eCollection 2014.

Effects of moxifloxacin exposure on the conjunctival flora and antibiotic resistance profile following repeated intravitreal injections.

Ataş M, Başkan B, Ozköse A, Mutlu Sarıgüzel F, Demircan S, Pangal E.

AIM: To evaluate the effects of moxifloxacin exposure on the conjunctival flora and antibiotic resistance profile following repeated intravitreal injections.

METHODS: Seventy-two eyes of 36 patients [36 eyes in control group, 36 eyes in intravitreal injection (IVI) group] were enrolled in the study. All the eyes had at least one IVI and had diabetic macular edema (DME) or age-related macular degeneration (ARMD). Moxifloxacin was prescribed to all the patients four times a day for five days following injection. Conjunctival cultures were obtained from the lower fornix via standardized technique with every possible effort made to minimize contamination from the lids, lashes, or skin. Before the application of any ophthalmic medication, conjunctival cultures were obtained from both eyes using sterile cotton culture. An automated microbiology system was used to identify the growing bacteria and determine antibiotic sensitivity.

RESULTS: The bacterial cultures were isolated from 72 eyes of 36 patients, sixteen of whom patients (44.4%) were male and twenty (55.6%) were female. Average age was 68.4±9.0 (range 50-86). The average number of injections before taking cultures was 3.1+1.0. Forty-eight (66.7%) of 72 eyes had at least one significant organism. There was no bacterial growth in 8 (20.5%) of IVI eyes and in 16 (44.4%) of control eyes (P=0.03). Of the bacteria isolated from culture, 53.8% of coagulase negative staphylococci (CoNS) in IVI eyes and 47.2% CoNS in control eyes. This difference between IVI eyes and control eyes about bacteria isolated from culture was not statistically significant (P=0.2). Eleven of 25 bacteria (44.0%) isolated from IVI eyes and 11 (57.9%) of 19 bacteria isolated from control eyes were resistant to oxacillin. The difference in frequency of moxifloxacine resistance between two groups was not statistically significant (12.0% in IVI eyes and 21.1% in control eyes) (P=0.44). There were no cases of resistance to vancomycin, teicoplanin and linezolid.

CONCLUSION: There was no difference in species of bacteria isolated from cultures, or in the frequency of resistance to antibiotics between eyes that had recurrent IVI followed by moxifloxacin exposure compared with control eyes. However, the number of eyes that had bacterial growth was higher in IVI group than in the control group.

PMID: 25349806 [PubMed] PMCID: PMC4206894

Other treatment & diagnosis

Biomed Opt Express. 2014 Sep 12;5(10):3568-77.

Fully automated detection of diabetic macular edema and dry age-related macular degeneration from optical coherence tomography images.

Srinivasan PP, Kim LA, Mettu PS, Cousins SW, Comer GM, Izatt JA, Farsiu S.

Abstract: We present a novel fully automated algorithm for the detection of retinal diseases via optical coherence tomography (OCT) imaging. Our algorithm utilizes multiscale histograms of oriented gradient descriptors as feature vectors of a support vector machine based classifier. The spectral domain OCT data sets used for cross-validation consisted of volumetric scans acquired from 45 subjects: 15 normal subjects, 15 patients with dry age-related macular degeneration (AMD), and 15 patients with diabetic macular edema (DME). Our classifier correctly identified 100% of cases with AMD, 100% cases with DME, and 86.67% cases of normal subjects. This algorithm is a potentially impactful tool for the remote diagnosis of ophthalmic diseases.

PMID: 25360373 [PubMed]

Proc Natl Acad Sci U S A. 2014 Oct 27. [Epub ahead of print]

DICER1/Alu RNA dysmetabolism induces Caspase-8-mediated cell death in age-related macular degeneration.

Kim Y, Tarallo V, Kerur N, Yasuma T, Gelfand BD, Bastos-Carvalho A, Hirano Y, Yasuma R, Mizutani T, Fowler BJ, Li S, Kaneko H, Bogdanovich S, Ambati BK, Hinton DR, Hauswirth WW, Hakem R, Wright C, Ambati J.

Abstract: Geographic atrophy, an advanced form of age-related macular degeneration (AMD) characterized by death of the retinal pigmented epithelium (RPE), causes untreatable blindness in millions worldwide. The RPE of human eyes with geographic atrophy accumulates toxic Alu RNA in response to a deficit in the enzyme DICER1, which in turn leads to activation of the NLRP3 inflammasome and elaboration of IL-18. Despite these recent insights, it is still unclear how RPE cells die during the course of the disease. In this study, we implicate the involvement of Caspase-8 as a critical mediator of RPE degeneration. Here we show that DICER1 deficiency, Alu RNA accumulation, and IL-18 up-regulation lead to RPE cell death via

activation of Caspase-8 through a Fas ligand-dependent mechanism. Coupled with our observation of increased Caspase-8 expression in the RPE of human eyes with geographic atrophy, our findings provide a rationale for targeting this apoptotic pathway in this disease.

PMID: 25349431 [PubMed - as supplied by publisher]

Ocul Immunol Inflamm. 2014 Oct 27:1-2. [Epub ahead of print]

The Significance of the Neutrophil/Lymphocyte Ratio as a Simple Indicator of Inflammation in Age-related Macular Degeneration.

Ilhan N, Daglioglu MC, Ilhan O, Coskun M, Tuzcu EA, Kahraman H, Keskin U.

PMID: 25347768 [PubMed - as supplied by publisher]

Ocul Immunol Inflamm. 2014 Oct 27:1-2. [Epub ahead of print]

Accurate Use of Neutrophil/Lymphocyte Ratio in Patients with Age-related Macular Degeneration.

Ozgonul C, Sertoglu E.

PMID: 25347699 [PubMed - as supplied by publisher]

Ocul Immunol Inflamm. 2014 Oct 27:1. [Epub ahead of print]

Value of Pentraxin3 (PTX3) in Patients with Neovascular Age-related Macular Degeneration.

Agilli M, Aydin FN, Cayci T, Gulcan Kurt Y.

PMID: 25347554 [PubMed - as supplied by publisher]

Pathogenesis

Mol Vis. 2014 Sep 19;20:1258-70. eCollection 2014.

Semaphorin 3A blocks the formation of pathologic choroidal neovascularization induced by transforming growth factor beta.

Bai Y, Liang S, Yu W, Zhao M, Huang L, Zhao M, Li X.

OBJECTIVE: Choroidal neovascularization (CNV) is a major cause of vision loss in retinal diseases such as age-related macular degeneration (AMD). Previously, we demonstrated that semaphorin3A (Sema3A), which is a chemorepellent guidance molecule, inhibited the formation of retina neovascularization. In the present study, we investigated the antiangiogenic effects of Sema3A on transforming growth factor beta (TGF-β) in vitro and in vivo.

METHODS: Enzyme-linked immunosorbent assays (ELISAs) were used to measure the TGF-β levels in the vitreous humor of patients with AMD and controls. Human umbilical vein endothelial cells (HUVECs) were used for the in vitro study, and a laser-induced CNV mouse model was prepared for the in vivo study. The HUVECs were incubated with TGF-β and Sema3A. The proliferation, migration, apoptosis, and tube formation of the cells were then measured using BrdU, Transwell, flow cytometry, and Matrigel assays, respectively, and the SMAD2/3 signaling pathways were analyzed using western blot analysis. The C57BL/6J mouse retina was exposed to a laser to induce choroidal neovascularization (CNV), and Sema3A was injected intravitreously. After 14 days, fundus fluorescein angiography was performed to evaluate the

leakage area of the CNV. The vascular endothelial growth factor (VEGF) and TGF-β concentrations in the retina-choroid complex were measured with ELISA. Components of the p38 mitogen-activated protein kinase (MAPK), extracellular signal-regulated kinase-1/2 (ERK1/2), c-Jun NH2-terminal kinase (JNK), and SMAD2/3 signaling pathways in the Sema3A-treated groups were analyzed using western blotting.

RESULTS: In this study, we first verified that the vitreous TGF-β level was higher in patients with neovascular AMD than in the controls. We also showed that Sema3A inhibited TGF-β-induced HUVEC proliferation, migration, and tube formation and inhibited the downstream SMAD2/3 signaling pathway. Sema3A also induced TGF-β-stimulated HUVEC apoptosis and inhibited the response of TGF-β in vitro. In vivo, the TGF-β level was increased in the CNV mouse model. Sema3A not only inhibited laser-induced CNV formation but also inhibited the uptake of VEGF and TGF-β. In the western blot analysis, Sema3A was shown to inhibit the phosphorylation of p38 MAPK, ERK1/2, and JNK and to inhibit the SMAD2/3 signaling pathway after Sema3A treatment in CNV mice.

CONCLUSIONS: Sema3A can be applied as a useful, adjunctive therapeutic strategy for preventing CNV formation.

PMID: 25352735 [PubMed - in process] PMCID: PMC4168834

Mol Vis. 2014 Sep 13;20:1253-7. eCollection 2014.

Complement factor I and age-related macular degeneration.

Alexander P, Gibson J, Cree AJ, Ennis S, Lotery AJ.

PURPOSE: The complement system has been implicated in the pathogenesis of age-related macular degeneration (AMD). Complement factor I (CFI) is a serum protease that inhibits all complement pathways. A previous multicenter study identified a single missense CFI mutation (p.Gly119Arg) in 20/3,567 (0.56%) of AMD cases versus 1/3,937 (0.025%) of controls, thus suggesting that this mutation confers a high risk of AMD. A second CFI mutation, p.Gly188Ala, was identified in one patient with AMD.

METHODS: We screened 521 unrelated AMD cases and 627 controls for the p.Gly119Arg and p.Gly188Ala variants. All participants were Caucasian and >55 years, and recruited through Southampton Eye Unit or research clinics in Guernsey. All participants underwent dilated fundal examination by an experienced retinal specialist. SNP assays were performed using KASP™ biochemistry.

RESULTS: The p.Gly119Arg mutation was identified in 7/521 AMD cases compared to 1/627 age-matched controls (odds ratio [OR] = 8.47, confidence interval [CI] = 1.04-69.00, p = 0.027). There was a varied phenotype among the seven cases with the mutation, which was present in 4/254 (1.6%) cases with active or end-stage wet AMD and 3/267 dry AMD cases (1.1%). The p.Gly188Ala substitution was identified in 1/521 cases and 1/627 controls.

CONCLUSIONS: Our results identified a much higher frequency of heterozygosity for p.Gly119Arg in both cases and controls than in previous studies. Of note is that our sub-cohort from Guernsey had a particularly high frequency of p.Gly119Arg heterozygosity in affected individuals (4%) compared to our sub-cohort from the mainland (0.71%). Although these data support the conclusions of van de Ven et al. that the p.Gly119Arg substitution confers a high risk of AMD, our data suggest that this missense mutation is not as rare or as highly penetrant as previously reported. There was no difference in frequency for a second CFI variant, p.Gly188Ala, between the cases and the controls.

PMID: 25352734 [PubMed - in process] PMCID: PMC4165324

Epidemiology

Int J Ophthalmol. 2014 Oct 18;7(5):872-8. eCollection 2014.

Iris color and associated pathological ocular complications: a review of epidemiologic studies.

Sun HP, Lin Y, Pan CW.

AIM: To elucidate the associations of iris color with major eye diseases.

METHODS: A systematic search on Medline with coverage up to August 2013 was conducted. Assessment of the quality of studies based on their levels of evidence was in accordance with the Centre for Evidence-Based Medicine, Oxford, United Kingdom.

RESULTS: A relationship between darker iris color and an increased risk of age-related cataract has been reported from cross-sectional studies and prospective cohort studies. There was no consistent evidence supporting a major role of iris color in the development or progression of age-related macular degeneration. The association of iris color with ocular uveal melanoma has been confirmed by a meta-analysis of observational studies previously. The etiologic synergism between light iris color and environmental exposure such as UV the exposure of UV radiation was found. There were no studies evaluating the refractive associations with iris color but there may be a possible link between iris color and myopia.

CONCLUSION: Darker iris color is associated with an increased risk of cataract and a reduced risk of ocular uveal melanoma. The association of iris color with age-related macular degeneration is not confirmed. Ophthalmologists should be aware that the risk of ocular disorders appears to vary by differences in iris color.

PMID: 25349810 [PubMed] PMCID: PMC4206898

Int J Ophthalmol. 2014 Oct 18;7(5):773-7. eCollection 2014.

Vascular endothelial growth factor gene polymorphisms in age-related macular degeneration in a Turkish population.

Bulgu Y, Cetin GO, Caner V, Cetin EN, Yaylali V, Yildirim C.

AIM: To assess the association between age-related macular degeneration (AMD) and three single nucleotide polymorphisms (SNPs) related to the vascular endothelial growth factor (VEGF) gene.

METHODS: The patients who were diagnosed with AMD were included in this prospective study. Three SNPs (rs1413711, rs2146323, and rs3025033) of the VEGF gene were genotyped by real-time polymerase chain reaction in the genomic DNA isolated from peripheral blood samples of the 82 patients and 80 controls.

RESULTS: The genotype frequencies of rs1413711 and rs2146323 were not significantly different between the study group and the control group (P=0.072 and P=0.058). However, there was a significant difference in the genotype frequencies of these SNPs between the wet type AMD and dry type AMD (P=0.005 and P=0.010, respectively). One of the SNPs (rs1413711) was also found to be associated with the severity of AMD (P=0.001) with significant genotype distribution between early, intermediate, and advanced stages of the disease. The ancestral alleles were protective for both SNPs while the polymorphic alleles increased the risk for dry AMD.

CONCLUSION: VEGF SNPs rs1413711 and rs2146323 polymorphisms are significantly associated with AMD subtypes in our population.

PMID: 25349791 [PubMed] PMCID: PMC4206879

Genetics

Mol Vis. 2014 Oct 17;20:1434-42. eCollection 2014.

Relationship between SERPING1 rs2511989 polymorphism and age-related macular degeneration risk: A meta-analysis.

Ma YB, Fu SY, Ma YH, Liu HL.

PURPOSE: We conducted a meta-analysis aiming to evaluate the relationship between a common polymorphism (rs2511989 G>A) in the SERPING1 gene and the risk of age-related macular degeneration (AMD).

METHODS: The PubMed, CISCOM, CINAHL, Web of Science, Google Scholar, EBSCO, Cochrane Library, and CBM databases were searched for relevant articles published before November 1, 2013, without any language restrictions. A meta-analysis was conducted using STATA 12.0 software. We calculated a crude odds ratio (OR) with a 95% confidence interval (95% CI) to evaluate the relationships under five genetic models.

RESULTS: Seven case-control studies with a total of 7,159 patients with AMD and 5,797 healthy subjects met the inclusion criteria. The results of our meta-analysis showed that the SERPING1 rs2511989 polymorphism might be correlated with an increased risk of AMD (G allele versus A allele: OR = 1.09, 95% CI = 1.03-1.15, p = 0.020; GG + GA versus AA: OR = 1.14, 95% CI = 1.03-1.26, p = 0.014; GG versus GA+AA: OR = 1.10, 95% CI = 1.02-1.19, p = 0.012; GG versus AA: OR = 1.20, 95% CI = 1.07-1.34, p = 0.002; respectively). Results of subgroup analysis by ethnicity revealed positive correlations between the SERPING1 rs2511989 polymorphism and risk of AMD among Caucasians under five genetic models (all p<0.05), but not among Asians (all p>0.05).

CONCLUSIONS: The current meta-analysis shows that the SERPING1 rs2511989 polymorphism may have a positive effect on the risk of AMD, especially among Caucasians.

PMID: 25352749 [PubMed - in process]

Diet & lifestyle

Mol Vis. 2014 Sep 11;20:1228-42. eCollection 2014.

Bioavailability of AREDS1 micronutrients from softgel capsules and tablets: a pilot study.

Johnson EJ, Vishwanathan R, Rasmussen HM, Lang JC.

PURPOSE: The benefits of antioxidant micronutrients in slowing progression to advanced stages of age-related macular degeneration (AMD) was supported by the 4/day tablet form investigated in the Age-related Eye Disease Study 1 (AREDS1) and the 2/day softgel form in the Age-related Eye Disease Study 2 (AREDS2). However, the choices of excipient, dosage form, and ingredient chemistry as well as the patient physiologies and pathologies can influence bioavailability and efficacy. The objective of the study was to explore the influence of dosage form on the bioavailability of the five primary AREDS1 and Tier-2 AREDS2 micronutrients: the metals zinc and copper, β-carotene, and vitamins E and C. The intent was to establish by chemical analysis the relative bioavailabilities of these five micronutrients in plasma, or serum for the metals, as well as to identify any opportunities for improvements.

METHODS: A total of 15 healthy men (5) and women (10) were recruited for a controlled, randomized, three-arm, crossover trial of the AREDS1 micronutrients. The study investigated responses in bioabsorption to a single dose of either four tablets or two softgels at the full dose level, or one softgel at the half-dose level. The bioavailability of each micronutrient was based on the pharmacokinetic profiles established through 15 samplings for each ingredient/dosage form in plasma/serum over the course of one week.

RESULTS: Bioavailability was estimated using model-independent and model-dependent procedures. A statistical advantage of the dosage form was observed in only two cases from the exaggerated effects using the half-dose softgel and for the tablet dosage form for β-carotene and vitamin E. An unanticipated complexity was suggested by the bimodal absorption of zinc. For these micronutrients, no disadvantage (though potential advantage) was inferred for the water-soluble components presented in a softgel formulation. Increased fractional absorption was observed for the smaller dose (one capsule versus two), but it was not sufficient to reach the level achieved by the full dose of either four tablets or two softgels. A

model-dependent analysis permitted an estimation of the percentage of micronutrients absorbed, with zinc, the single most important ingredient, absorbed at about a 10% level.

CONCLUSIONS: The results suggest modestly contradictory requirements in the dosage form for water-soluble and lipid-soluble ingredients, as based on a goal of improved bioavailability. Comparative consistency in bioavailability was observed across dosage forms, and most nutrients between AREDS1 and AREDS2 (full dose) formulations relative to the significant variations observed within this controlled population. The results emphasize the importance of defining the requisite bioavailability of each micronutrient and the influence of the dosage form that provides it. With the recognition of global and population-specific micronutrient deficiencies, notably in the elderly populations afflicted with AMD and their significant metabolic and health consequences, establishing efficient means of supplementation are of continuing epidemiologic interest.

PMID: 25352732 [PubMed - in process] PMCID: PMC4164907

Ophthalmic Res. 2014 Oct 25;52(4):198-205. [Epub ahead of print]

Role of Lutein Supplementation in the Management of Age-Related Macular Degeneration: Meta-Analysis of Randomized Controlled Trials.

Wang X, Jiang C, Zhang Y, Gong Y, Chen X, Zhang M.

Objective: The conduct of this meta-analysis aimed at examining the individual role of lutein as a dietary supplement in improving conditions of age-related macular degeneration (AMD) from the data generated from randomized controlled trials (RCTs).

Method: The literature search was made in multiple electronic databases. Eligibility criteria were RCTs that recruited AMD patients or individuals at risk and evaluated lutein supplementation efficacy against placebo. The quality of the trials was assessed by using the Jadad scale. The meta-analysis was conducted under the fixed effect model with RevMan software by calculating the mean differences of the changes from baseline of both lutein and placebo groups. Parameters of interest were macular pigment optical density (MPOD) and visual acuity (VA) in logMAR (minimum angle of resolution). Heterogeneity was determined by $\chi 2$ and I2 and publication bias was assessed by visual examination of funnel plots.

Results: After following predetermined inclusion and exclusion criteria, five RCTs that recruited 445 participants were selected for the meta-analysis. It has been found that lutein treatment was associated with a significant improvement in MPOD, with mean differences between lutein and placebo groups in the changes from baseline of 0.09 (95% CI: 0.06, 0.12; $p < 0.00001$). VA also improved with a mean difference between lutein and placebo groups in the changes from baseline of -0.04 (95% CI-0.07, 0.00; $p = 0.05$). Statistical heterogeneity was not apparent.

Conclusion: A statistically highly significant effect of lutein supplementation has been observed for improving the MPOD, whereas the improvement in VA was milder. A daily dose of 10 mg was found as effective as higher doses in this meta-analysis. However, the number of input studies is not adequate for conclusive evidence.

PMID: 25358528 [PubMed - as supplied by publisher]

Measuring Health-Related Quality of Life for Patients with Diabetic Retinopathy [Internet].

Editors: Milne A, Johnson JA, Tennant M, Rudnisky C, Dryden DM.

Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Apr. Report No.: DBTR0610.

AHRQ Technology Assessments.

OBJECTIVES:To identify and evaluate the psychometric properties of tools used to measure health-related quality of life (HRQL) in patients receiving treatment for diabetic retinopathy (DR), and to assess the effectiveness of interventions for DR to improve HRQL.

DATA SOURCES:We conducted a systematic and comprehensive search in six electronic databases and hand searched reference lists of reviews and included studies.

REVIEW METHODS:Study selection, quality assessment, and data extraction were completed by reviewers independently and in duplicate. We included articles that presented data on HRQL outcomes following an intervention for DR (including diabetic macular edmema (DME). Mean differences and 95 percent confidence intervals were calculated for continuous outcomes. We did not conduct any meta-analyses due to heterogeneity.

RESULTS:We identified four validated HRQL measures: 36–Item Short Form Health Survey (SF–36), National Eye Institute Visual Functioning Questionnaire (VFQ–25 and –51), Visual Function Index (VF–14), and Diabetes Treatment Satisfaction Questionnaire (DTSQ). We also identified two tools that are currently undergoing evaluation: the Retinopathy Treatment Satisfaction Questionnaire (RetTSQ) and the Retinopathy Dependent Quality of Life (RetDQoL). Two randomized controlled trials (RCTs) reported on HRQL outcomes following anti-vascular endothelial growth factor (anti-VEGF) treatment for DME. Seven observational studies reported on HRQL outcomes following: laser photocoagulation (two), vitrectomy (two), panretinal photocoagulation versus vitrectomy (one), and phacoemulsification cataract surgery (two). The RCT comparing pegaptanib sodium versus sham reported a statistically significant improvement from baseline for the composite score of the VFQ–25 at 2 years (but not at 1 year). The three-arm RCT comparing ranibizumab monotherapy versus ranibizumab plus laser versus laser showed a statisitically significant difference for the composite score of the VFQ–25 for both anti-VEGF arms versus laser at 1 year. The strength of evidence for anti-VEGF was assessed as low. For the remaining interventions, the studies were at high risk of bias due to weak study designs (before-after and cohort studies) and poor implementation. There is insufficient evidence to determine whether one of these treatments for DR is more effective than another in improving HRQL in this patient population.

CONCLUSIONS:We identified few HRQL measurement instruments that have been used to assess the impact of treatment in patients with DR or DME; however, the tools that have been used have been adequately evaluated. Two tools developed specifically for patients with DR are currently undergoing evaluation. In general, HRQL was improved following interventions for DR. Further research on HRQL following anti-VEGF treatment for DME is needed to confirm the results of two RCTs. The current research on the impact of other interventions for DR on HRQL is insufficient to draw conclusions about the relative effect of one intervention versus another. RCTs that assess the impact of treatments for DR should include HRQL as an outcome.

PMID: 25356446 [PubMed]