Where's the Evidence? A look at the role of nutrition in AMD

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Learning Objectives:
• To help educate on what ocular vitamins and nutrients have been shown to be beneficial in prevention of ocular conditions, particularly
• To recognize what patients will benefit from these therapies and which ones will not
• To recognize the potential side effects of the ocular vitamins and nutrients and potential complications with certain systemic conditions
• To review what the current literature is saying about ocular vitamins and nutrients in 2013
• To recognize how ocular nutrition can be integrated into a primary care practitioners practice

Presentation Outline and Key Points/Take Homes

I. Role of Ocular Nutrition in Primary Eye Care
   • Prevention
   • Historical view on the role nutrition in eye care
   • Current view on the role of nutrition in eye

II. AMD and nutrition, a review of the current evidence
   • 2014 = practicing preventative medicine for AMD and other eye conditions
     o Disease burden of AMD is rising world wide
   • How the pathophysiology and nutrition in AMD coincide
     o Modifiable vs. non – modifiable risk factors
       ▪ Modifiable – Smoking, chronic sunlight exposure, obesity, high blood pressure, high Cholesterol, poor nutrition
       ▪ Non-modifiable - Age-associated, GENETICS and family history, Caucasian
       ▪ Nutrition influence on pathophysiology - Among environmental factors, smoking, obesity and dietary factors, including antioxidants and dietary fat intake influence onset and progression of AMD.
       o Review of AREDS 1
         ▪ 20% risk reduction in vision loss for patients with intermediate AMD
         ▪ 25% risk reduction to advanced AMD for patients with intermediate AMD
         ▪ Take home point: despite the vitamins; patients will still progress

III. AREDS 2 Update Did the results change our clinical practice?
CONCLUSIONS – Revised Formula
- Vitamin C (500 mg)
- Vitamin E (400 IU)
- Lutein (10 mg)/Zeaxanthin (2 mg)
- Zinc (80 mg zinc oxide)
- Copper (2 mg cupric oxide)

Nutrition’s impact on AREDS 2
- Diabetes: 13%
- Smoking Status: 50% former/7% current
- Participants in the study had three to four times the average lutein and zeaxanthin intake of average Americans
- Harvard Dietary Assessment
  - Baseline dietary intake of study nutrients were taken
  - Highly nourished – received higher scores than average American population
- Serum levels at baseline
  1. Took serum levels of nutrients at baseline and 1,3 and 5 year follow-ups
  2. Compared with National Health and Nutrition Examination Survey
  - This cohort had statistically significant higher serum levels of nutrients than average

Omega 3 supplements vs. dietary Omega-3s:
- There are many studies that show the benefit of Omega-3s which contradicts the results seen in AREDS 2
- Studies that prove efficacy are MOSTLY DIETARY
- Other considerations:
  - Healthy cohort- additive benefit of adding more EPA/DHA into people's diet that were already getting enough?
  - Triglyceride vs. Ethyl ester
  - Dosage – varying thoughts – high dose of DHA is shown to be beneficial to retina – only 350 mg was used in AREDS2
  - NAT-1 and NAT-2 Study studied higher supplementation dosages
  - May be greater evidence if look at patients with long-term sustained levels of omega-3

The Zinc controversy
- What should we be recommending 80 mg vs. 25 mg
  - High levels of zinc have been associated with side effects of different severity – stomach upset to increased risk of cancer to alzheimers
  - The recommendation for the amount of zinc was not clear in the AREDS 2 review by Dr. Chew because both amounts were found to be adequate
Clinical Implications
- AREDS2 is only valid for a small subset of patients (bilateral, intermediate or advanced AMD)
- Even with AREDS patients are going to progress
- 25% reduced risk, extra 26% reduced risk = 33% reduced risk
- **We need to educate our patients on PREVENTION**
- AMD is a chronic disease and we as optometrists can play a huge role!
- We know that eating healthy improves eye health – we need to educate our patients on this before they develop changes

V. Nutrition and Prevention of AMD
- Dietary antioxidants
  - Lutein and Zeaxanthin (Carotenoids)
    - Growing body of evidence to support dietary intake of carotenoids and prevention of AMD
    - Consistent evidence that participants with > 2 risk alleles of either or both of the CFH or ARMS2 had a significantly reduced risk of early or any AMD if they frequently consumed food items rich in LZ.
    - Increased dietary lutein and Zeaxanthin and macular pigment optical density
    - Improved visual function with carotenoids
  - Dietary Omega-3s
- Clinical Implications:

IV. Nutrigenomics – Do Genetics matter
- The study of effects of foods and food constituents on gene expression
- May help direct what supplementation to give to each individual patient
  - Clarify Omega-3s, Zinc, Vitamin A,C,E dosage
  - Clarify dosage nutrients for all ocular diseases that may respond
    - Seddon 1994:
    - Awh vs. Chew genotype analysis from AREDS 2
- Carl Awh, MD has published that there is a demonstrated role for genotype-directed nutritional therapy in patients with moderate age-related macular degeneration (AMD)
  - Looked at two genetic polymorphisms Complement Factor H (CFH) and ARMS 2
  - Subjects who have 1 or 2 CFH risk alleles were more likely to benefit from the use of antioxidant supplements alone, rather than the full AREDS supplement
• In these patients, treatment with zinc, either alone or as a component of the AREDS formulation, was associated with increased AMD progression compared to treatment with antioxidants alone.

• Emily Chew, MD claims that an alternative statistical analysis performed by the National Eye Institute failed to find sufficient evidence to support genetic testing for this indication.

• AWH conclusions: Individuals with moderate AMD could benefit from pharmacogenomic selection of nutritional supplements. In this analysis, patients with no CFH risk alleles and with 1 or 2 ARMS2 risk alleles derived maximum benefit from zinc-only supplementation. Patients with one or two CFH risk alleles and no ARMS2 risk alleles derived maximum benefit from antioxidant-only supplementation; treatment with zinc was associated with increased progression to advanced AMD. These recommendations could lead to improved outcomes through genotype-directed therapy.

• CHEW conclusions: Conclusions: The AREDS supplements reduced the rate of AMD progression across all genotype groups. Furthermore, the genotypes at the CFH and ARMS2 loci did not statistically significantly alter the benefits of AREDS supplements. Genetic testing remains a valuable research tool, but these analyses suggest it provides no benefits in managing nutritional supplementation for patients at risk of late AMD.

• Importance of good methodology

  • Awh did a subgroup analysis with a similar design to Chew's analysis, dividing AREDS study patients into nine separate genotype groups.
  • Demonstrated that this method was statistically underpowered even to demonstrate that AREDS supplements were better than placebo.

• Contrasting Study Findings:
  • Another important paper by Klein et al. reported that supplementation with AREDS antioxidants plus zinc resulted in a greater reduction in AMD progression (68%) in those with the low-risk genotype for CFH than in those with the high-risk genotype (11%).
  • This interaction was primarily related to the zinc component of the supplements.
  • While the major benefit of zinc and antioxidants was seen in patients with the low-risk CFH genotype, all CFH genotypes (both high and low risk) benefited from zinc and antioxidants. Importantly, no harm was seen in those with CFH risk alleles. The authors also found no association between AREDS treatment assignment and having ARMS2 risk alleles.
  • Difficulties for developing good methodology for studying nutrition.

• Clinical Implications:
  o Due to the inconsistent methods and results, there is currently insufficient information to personalize recommendations for supplement use based on genotype.
  o Current conclusions from the American Academy of Ophthalmology task force for genetics recommends avoiding routine genetic testing for...
genetically complex disorders like AMD until specific treatment or surveillance strategies have been shown in published trials to be of benefit to individuals with specific genotypes.

V. Conclusions

- Even with AREDS and nutrition, AMD patients are going to progress
  - 25% reduced risk, extra 26% reduced risk = 33% reduced risk
- **We need to be educating our patients on PREVENTION**
  - AMD is a chronic disease and we as optometrists can play a huge role!
    - We know that eating healthy improves eye health – we need to educate our patients on this BEFORE they develop changes
    - Studies looking at dietary levels seem to have strongest evidence for prevention

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