關於JAMA(2013)第19期葉黃素與玉米黃素之研究

◎文／藥師曾美容

有關藥師週刊1828期第5版「繼續教育國際化 讓藥師專業更提升」一文中，提及葉黃素和玉米黃素能降低老年黃斑病變發展風險一事，爲提供正確資訊，茲將文中結論摘譯給全體藥師知悉。

本文在探討葉黃素、玉米黃素和omega-3（ω-3）是否能降低老年黃斑病變（AMD）的發展風險，因此研究設計分成4組，每個受試者除了都要服用AREDS補充配方外，參與者被隨機分配再接受葉黃素10 mg＋玉米黃素 2 mg、DHA 350 mg＋EPA 650 mg、葉黃素＋玉米黃素＋DHA＋ EPA、安慰劑。AREDS補充配方：抗氧化劑維生素C 500 mg＋維生素E 400 IU＋ β-胡蘿蔔素 15 mg＋鋅 80 mg (ZnO)＋Cu 2 mg (CuO)。

另外所有的參與者也被要求攝取原始AREDS 配方或接受二次隨機，服用變化的AREDS 配方（除去 β-胡蘿蔔素或降低鋅的劑量），或兩者。

結果顯示

1608個參加者，1940隻眼，追蹤期中位數爲5年，是否進展到惡化的AMD。依據Kaplan-Meier 概率，5年發展成惡化的AMD，安慰組爲31%（406人，493隻眼），葉黃素＋玉米黃素組爲29%（ 399人，468 隻眼），DHA + EPA爲31%（416人，507隻眼），葉黃素+玉米黃素＋DHA + EPA爲30%（387人，472隻眼）。

與安慰組比較，進展到惡化的AMD，主要分析，顯示無統計學顯著減少（葉黃素+玉米黃素組：風險比 (HR) 0.90，98.7%CI，0.76-1.07，P= 0.12；DHA + EPA：HR= 0.97，98.7% CI，0.82-1.16，P=.70；葉黃素+玉米黃質＋DHA + EPA：HR=0.89，98.7% CI，0.75-1.06，P= 0.10。

除去 β-胡蘿蔔素或低劑量鋅，對發展成惡化的AMD沒有明顯的影響。但值得注意的是 β-胡蘿蔔素組比沒有 β-胡蘿蔔素組有更多的肺癌，23 (2.0%) vs.11 (0.9%)，P = 0.04，主要發生在過去吸菸者。

結論

將葉黃素+玉米黃素、DHA+ EPA、或兩者添加至 AREDS 配方中，在主要分析，並沒有進一步降低進展成惡化的AMD的風險。然而，由於過去吸煙者肺癌的發生率潛在增加，葉黃素+玉米黃素可以取代 AREDS 配方中的類胡蘿蔔素是適當的。

資料來源：

Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA. 2013 May 15;309(19):2005-15. doi: 10.1001/jama.2013.4997.

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Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial.

Age-Related Eye Disease Study 2 Research Group.

Collaborators (23)

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Abstract

IMPORTANCE: Oral supplementation with the Age-Related Eye Disease Study (AREDS) formulation (antioxidant vitamins C and E, beta carotene, and zinc) has been shown to reduce the risk of progression to advanced age-related macular degeneration (AMD). Observational data suggest that increased dietary intake of **lutein** + zeaxanthin (carotenoids), omega-3 long-chain polyunsaturated fatty acids (docosahexaenoic acid [DHA] + eicosapentaenoic acid [EPA]), or both might further reduce this risk.

OBJECTIVES: To determine whether adding **lutein** + zeaxanthin, DHA + EPA, or both to the AREDS formulation decreases the risk of developing advanced AMD and to evaluate the effect of eliminating beta carotene, lowering zinc doses, or both in the AREDS formulation.

DESIGN, SETTING, AND PARTICIPANTS: The Age-Related Eye Disease Study 2 (AREDS2), a multicenter, randomized, double-masked, placebo-controlled phase 3 study with a 2 × 2 factorial design, conducted in 2006-2012 and enrolling 4203 participants aged 50 to 85 years at risk for progression to advanced AMD with bilateral large drusen or large drusen in 1 eye and advanced AMD in the fellow eye.

INTERVENTIONS: Participants were randomized to receive **lutein** (10 mg) + zeaxanthin (2 mg), DHA (350 mg) + EPA (650 mg), **lutein** + zeaxanthin and DHA + EPA, or placebo. All participants were also asked to take the original AREDS formulation or accept a secondary randomization to 4 variations of the AREDS formulation, including elimination of beta carotene, lowering of zinc dose, or both.

MAIN OUTCOMES AND MEASURES: Development of advanced AMD. The unit of analyses used was by eye.

RESULTS: Median follow-up was 5 years, with 1940 study eyes (1608 participants) progressing to advanced AMD. Kaplan-Meier probabilities of progression to advanced AMD by 5 years were 31% (493 eyes [406 participants]) for placebo, 29% (468 eyes [399 participants]) for **lutein** + zeaxanthin, 31% (507 eyes [416 participants]) for DHA + EPA, and 30% (472 eyes [387 participants]) for **lutein** + zeaxanthin and DHA + EPA. Comparison with placebo in the primary analyses demonstrated no statistically significant reduction in progression to advanced AMD (hazard ratio [HR], 0.90 [98.7% CI, 0.76-1.07]; P = .12 for **lutein** + zeaxanthin; 0.97 [98.7% CI, 0.82-1.16]; P = .70 for DHA + EPA; 0.89 [98.7% CI, 0.75-1.06]; P = .10 for **lutein** + zeaxanthin and DHA + EPA). There was no apparent effect of beta carotene elimination or lower-dose zinc on progression to advanced AMD. More lung cancers were noted in the beta carotene vs no beta carotene group (23 [2.0%] vs 11 [0.9%], nominal P = .04), mostly in former smokers.

CONCLUSIONS AND RELEVANCE: Addition of **lutein** + zeaxanthin, DHA + EPA, or both to the AREDS formulation in primary analyses did not further reduce risk of progression to advanced AMD. However, because of potential increased incidence of lung cancer in former smokers, **lutein** + zeaxanthin could be an appropriate carotenoid substitute in the AREDS formulation.

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