Vitamin and mineral supplements

Antioxidants are recommended for AMD due to oxidative stress on photoreceptors in the retina and the fact that cumulative damage caused by blue light enhances free radical production.

It has been proposed that antioxidants may prevent cellular damage in the retina by reacting with free radicals $\frac{(36)}{}$.

The substances that possess antioxidant activity are vitamins C and E, beta-carotene and some minerals, such as zinc, copper, selenium and manganese.

Some studies indicate that diets rich in antioxidants may protect against the appearance of signs of early AMD; in common perception, a diet rich in antioxidants is capable of protecting against AMD.

Randomised control trials and observational studies have been conducted in well-nourished Western populations; however, the role of dietary antioxidants in the primary prevention of AMD remains unclear.

In the 90's, several studies reported a protective effect against AMD development for high intakes of antioxidant vitamins and minerals.

In 1993, the EDCCS (Eye Disease Case-Control Study), performed a comparison between 421 patients with neovascular age-related macular degeneration and 615 control subjects, the results revealed that high plasma levels of antioxidants (vitamins A, C, E, selenium and carotenoids) are associated with a lower risk of developing neovascular AMD.

Additional carotenoid intakes, particularly of those present in the retina, are associated with a lower risk of developing $AMD^{(37)}$.

In 1994, the authors of the Baltimore Longitudinal Study on Aging, a study involving 976 patients, reported a protective effect against AMD for high plasma concentrations of Vitamin E.

The authors also found an antioxidant combination of Vitamin C, Vitamin E and beta-carotene to be protective $\frac{(38)}{}$.

In 1998, the Beaver Dam Eye Study, in which a cohort of 1,700 patients was subject to a 5-year follow-up eye examination, showed that a high intake of carotenoids and vitamin E is associated with a lower risk of developing large drusen.

High dietary zinc intakes would be associated with a lower number of retinal pigment epithelium anomalies $\frac{(39)}{}$.

In 2001, AREDS report no. 8, a large multicentric, randomised clinical trial, revealed that the risk of progression to advanced AMD was reduced by 28% in patients with intermediate AMD treated with high doses of antioxidant supplements (vitamins C and E, zinc and β -carotene), when compared to the placebo group (odds ratio: 0.72; 99% confidence interval: 0.52-0.98).

This study did not specifically investigate whether antioxidant supplements were effective in the primary prevention of early AMD in individuals without signs of this condition $\frac{(40)}{(40)}$.

In 2004, AREDS report no. 13 evaluated mortality rates in patients with ocular disorders taking high doses of antioxidants or zinc.

Results showed that mortality was lower in patients taking zinc (alone or with antioxidants) (12% reduction), when compared to those not taking this mineral (RR: 0.73; 95% CI: 0.61-0.89) $\frac{(41)}{}$.

In 2005, the Rotterdam Study, a population-based study involving 4170 participants, showed that an above-average intake of the 4 AREDS trial nutrients protected against AMD development or early AMD, as indicated by large drusen, and was associated with a 35% reduction in the risk of AMD (HR: 0.65; 95% CI: 0.46-0.92) $\frac{(42)}{}$.

In 2007, Chong and colleagues undertook a systematic review and meta-analysis of nine prospective cohort studies and three randomised clinical trials.

The results from the first studies indicated that vitamin A, vitamin C, vitamin E, zinc, L, Z, alpha-carotene, beta-carotene, beta-cryptoxanthin and lycopene have little or no effect in the primary prevention of early AMD.

The three randomised clinical trials failed to show that antioxidant supplements prevented early $AMD^{(43)}$.

In 2008, a systematic review and meta-analysis undertaken with the objective of examining available evidence as to whether antioxidant vitamin or mineral supplements are able to prevent AMD development or delay its progression was published online.

No evidence was found that antioxidant (vitamin E or beta-carotene) supplements are able to prevent AMD (RR 1.03; 95% CI; 0.74-1.43).

Some evidence was found that antioxidant (beta-carotene, vitamin C and E) and zinc supplements were able to delay progression to advanced AMD and prevent loss of visual acuity in individuals displaying signs of the disease (adjusted odds = 0.68; 95% CI: 0.53-0.57, and 0.77; 95% CI: 0.62-0.96, respectively) $\frac{(44)}{1}$.