

# A randomised, double masked, clinical trial of high dose vitamin A and vitamin E supplementation after photorefractive keratectomy

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## Abstract

**Aim**—To evaluate the effect of a high dose vitamin A and E supplementation on corneal re-epithelialisation time, visual acuity and haze following photorefractive keratectomy (PRK).

**Methods**—Two groups of 20 patients who underwent myopic PRK were supplemented with either 25 000 IU retinol palmitate and 230 mg  $\alpha$  tocopheryl nicotinate or a placebo. Clinical outcomes were evaluated up to 360 days.

**Results**—In the vitamin treated group, re-epithelialisation time was significantly faster ( $p=0.029$ ) and haze incidence was reduced ( $p=0.035$ ), especially for high myopic corrections ( $p=0.043$ ). This group also reported a significantly better uncorrected visual acuity ( $p=0.043$ ).

**Conclusions**—High dose vitamin A and E oral supplementation may accelerate re-epithelialisation time and may reduce corneal haze formation after PRK.

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Corneal haze and myopic regression are the main undesirable complications after excimer laser treatment.<sup>1</sup> In the past few years, several authors indicated that keratocytes and epithelial cells are mainly involved in the healing response. In particular, it was suggested that the disappearance of anterior stromal keratocytes in response to excimer laser surgery was an initiating factor, which could lead to epithelial hyperplasia and eventually to haze formation and regression.<sup>2</sup> Wilson showed that anterior keratocyte death was mediated by apoptosis with little accompanying inflammation, while Shimmura indicated the generation of free radicals as the main cause of apoptosis, together with other triggers. In particular, the hydroxyl radical (OH•) was identified as the specific oxygen species of radicals formed by the excimer laser.<sup>3,4</sup>

The extent of tissue damage, therefore, may reflect the balance between the oxidative damage and the local antioxidation defence system and there is considerable experimental evidence on animals to support the use of pharmacological agents, which are specifically directed against the oxygen radicals that are formed during excimer photoablation or could influence corneal epithelial proliferation and differentiation.<sup>5,6</sup>

On this basis, we tried to verify the applicability of these data from animal models to the human cornea and we therefore

performed this study to determine whether the use of a high dose vitamin A and E supplementation could improve corneal re-epithelialisation, and reduce the incidence of haze and myopic regression after PRK.

## Materials and methods

Between February and April 1999, all patients requesting excimer laser surgery for myopia at the eye clinic, department of ophthalmology, University of Bari, Italy were considered eligible for the study. The independent ethic committee of the Policlinico, Bari, Italy, approved the study and written informed consent was obtained from all patients. Preoperative assessment consisted of a complete ophthalmic examination. Inclusion criteria were age ranging from 20-30 years, stable refraction for at least 2 years, myopia within -2 to -10 D, regular astigmatism and best corrected visual acuity higher than 0.2 reported on the logarithm of the minimum angle of resolution (logMAR) scale.<sup>7</sup> We excluded from the study patients with an history of ocular disease, previous refractive treatment, contact lens wear in the previous 2 months, intolerance to one of the components of the test capsules, wound healing abnormalities (for example, keloids), gastroenteric diseases, systemic diseases (especially diabetes, cardiac diseases and coagulation disorders because vitamin E could inhibit cytochrome P 450, enhancing the effects of insulin, digital and oral anticoagulants).<sup>8</sup>

Forty patients (40 eyes) met all the preoperative criteria and were randomly assigned either to the treated (vitamin group) or to the control group (20 patients each). The vitamin group received an oral supplementation of vitamin A (25 000 IU retinol palmitate) and vitamin E (230 mg  $\alpha$  tocopheryl nicotinate), (Evitex capsules, Alcon, Milan, Italy) whereas the control group was given a placebo capsule of the same colour and aspect.

## SURGICAL TECHNIQUE

All surgical procedures were performed by the same surgeon (MV), using Laserscan 2000 (Lasersight, Orlando, FL, USA), a flying spot excimer laser, whose technical features and surgical procedure are described elsewhere.<sup>9</sup> Corneal de-epithelialisation was carried out using a 20% alcoholic solution.

## POSTOPERATIVE SELECTION AND EVALUATION

On removal of the soft contact lens, all patients received a topical steroid treatment, dispensed four times a day for 1 month and therefore in

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considered acceptable, even though further clinical studies are desirable.

In conclusion, this pilot study demonstrates that vitamin A and E administration in the first 3 months following excimer laser surgery significantly reduces the incidence of haze formation and myopic regression. This could confirm that free radical levels are an important determinant of the clinical outcome of excimer laser surgery. We therefore believe that concurrent antioxidant therapy may positively influence corneal wound healing after excimer laser keratectomy, although further studies are obviously required.

The authors have no proprietary interest in the development or marketing of any product or instrument mentioned in this article.

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