

# Tear film changes after antioxidant supplementation in type 2 diabetes mellitus

Priyanka P. Doctor, S. Kalpana, S. Viswanathan, Rahul P. Doctor

Department of Ophthalmology, Sri Ramachandra Medical College and Research Institute, Chennai (A Harvard Medical International Associated Institute), India

**BACKGROUND:** To study the effect of supplementation with vitamin C and E on tear film parameters in diabetic patients. **METHODOLOGY:** Fifty patients were enrolled in the study. The patients were given vitamin C (1,000 mg/day) and vitamin E (400 IU/day) for 10 days. Schirmer test and Tear film Break-Up Time (BUT) were performed. **RESULTS:** Supplementation was accompanied with improved values for the Schirmers test ( $P < 0.001$ ) and BUT. **CONCLUSIONS:** Diabetes mellitus is associated with increased oxidative stress. Our study suggests that supplementation with antioxidant vitamins C and E probably plays an important role in improving the ocular surface.

**KEY WORDS:** Break-up time, oxidative stress, Schirmer test

supplementation with orally administered vitamins C and E on 'tear film'-related clinical parameters in diabetic patients.

## Methodology

Fifty patients with type 2 diabetes mellitus (DM) - 25 men and 25 women - mean age 67.3 years (range 45-82 years), were recruited from the Department of Ophthalmology at the Sri Ramachandra Medical College and Research Institute, Chennai. A total of 100 eyes were studied between April and May 2005. Clinical data were collected regarding the duration of DM, the levels of glycosylated hemoglobin (HbA<sub>1c</sub>), medications, existence of diabetic neuropathy, existence and stage of diabetic retinopathy and smoking status [Table 1]. The status of diabetic retinopathy was assessed by fundus examination and, if necessary, by fluorescein angiography.

## Introduction

Ocular surface changes and tear film abnormalities are well-established manifestations of ocular surface diabetic disease.<sup>[1-3]</sup> The conjunctival epithelium, is a non-keratinizing, stratified squamous tissue which undergoes constant reorganization with continuous loss of terminally differentiated superficial cells and basal cell proliferation.<sup>[4]</sup> Owing to its exposed nature, the ocular surface is at particular risk of oxidative damage by environmental and photo-induced oxidative stress.<sup>[5]</sup> The tear film is very rich in various antioxidants which protect the external surface of the eye.<sup>[6]</sup> Diet is important in controlling the homeostatic balance of the ocular physiological function.<sup>[7]</sup>

In the present study, we studied the effect of antioxidant

The following exclusion criteria were applied:

- Systemic disease other than DM
- Systemic medications that could interfere with tear film parameters
- Topical eye medications within the past 6 months
- Previous ophthalmic surgical or laser procedures
- Eye diseases other than dry eye and/or diabetic retinopathy
- History of taking vitamin supplements

**Table 1: Patient characteristics**

Age (years)	67.3 ± 11/7
Sex (Males/females)	25/25
Duration of diabetes (yrs)	13.22 ± 8.2
Therapy (OHA/Insulin)	32/18
HbA <sub>1c</sub> (%)	9.44 ± 1.82
Smoking (Yes/no)	10/40
Neuropathy (Yes/no)	20/30
Retinopathy (Yes/no)	38/12

Correspondence to Dr. Priyanka P. Doctor, 62, Chitrakoot, Altamount Road, Mumbai - 400 026, India.  
E-mail: priyanka.doctor@gmail.com

All patients were given oral vitamin C (1,000 mg/day) and vitamin E (400 IU/day) for 10 days. The patients entered the study after informed consent was obtained.

Tests were performed on the patients by the same investigator before and after vitamin supplementation, in the following order:

#### **Tear film Break-Up Time (BUT)<sup>[8]</sup>**

Moistened fluorescein strips were introduced into the conjunctival sac with minimal stimulation and the patients instructed to blink several times. The interval between the last complete blink and the appearance of the first corneal black spot in the stained tear film was measured three times and mean value calculated. BUT values less than 10 s were considered abnormal.

#### **Schirmer test<sup>[9]</sup>**

The standard Schirmer I test without anesthesia was performed by inserting the short portion of commercially obtained standard strips of precut filter papers bent at the notch, in the lateral third of the lower lid margin. The filter paper was left in place for 5 min; and after removal, the length of the dampened part was measured in mm from the notch distally. A measurement of 10 mm or less was considered abnormal.

The paired t-test was used to compare the measured parameters before and after vitamin supplementation. A probability level less than 5% was considered statistically significant.

### **Results**

Schirmer test and the BUT score improved after vitamin C and E supplementation [improved values after C and E supplementation: (11.64 ± 7.34 mm vs. 15.04 ± 7.22 mm,  $P < 0.001$ ), as well as the BUT score (median 10.4 s, range 5-25 vs. 13.7 s, range 8-27,  $P = 0.001$ )].

We also found that age of the patient and duration of DM adversely affected improvement in the measured values for BUT during vitamin administration ( $P < 0.05$ ).

Statistical analysis demonstrated that patients older than 65 years and/or with a duration of DM greater than 15 years showed less improvement in the measured parameters.

The presence of diabetic neuropathy did not correlate with changes statistically.

Mild to moderate, statistically significant correlations were detected between the changes in the Schirmer test ( $P < 0.001$ ) and BUT values ( $P = 0.001$ ).

### **Discussion**

These results demonstrate a clearly beneficial effect of orally administered antioxidant vitamins C and E in various clinical parameters of the tear film in diabetic patients. The vitamin supplementation improves tear film stability (BUT), tear secretion and volume (Schirmer test).

Several clinical and experimental studies have reported structural, metabolic and functional abnormalities in the conjunctiva and cornea of diabetic patients.<sup>[10-13]</sup>

Dogru *et al.*<sup>[2]</sup> compared non-insulin dependent patients with normal subjects and found that BUT and Schirmer test values were significantly lower in the DM group and were accompanied with goblet cell loss and conjunctival squamous metaplasia.

DM is associated with increased oxidative stress and free radical production.<sup>[14,15]</sup> Free radicals attack and damage critical cellular components, such as plasma membranes, which can lead to cell lysis. Hence free radicals can damage conjunctiva and lacrimal glands.<sup>[16]</sup> Moreover, studies in individuals with DM have detected ascorbic acid deficiency. It is well known that vitamins C and E can restore each other's antioxidant activity. The antioxidant potential of vitamins C and E can probably fortify ocular surface antioxidant defenses and eliminate the harmful effects of increased free radical production. Previous studies have reported similar results.<sup>[7]</sup>

Age of the patient and duration of DM are also reported to correlate with decreased corneal and conjunctival sensitivity.<sup>[2]</sup> This is consistent with our results, where we observed that patients older than 65 demonstrated diabetic neuropathy in a greater percentage than patients younger than 65 (62.7% vs. 34.3%).

In our study, Schirmer test changes also correlated with BUT changes, which probably results from the water-retentive properties of mucins.<sup>[17]</sup>

### **Conclusions**

Our study suggests that dietary elements such as vitamin C and vitamin E, which are usually reduced in DM, probably play an important role in improving the ocular surface.

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