Micronutrient supplementation with alpha lipoic acid, vitamin B1, vitamin B2 and rutin improves contrast sensitivity in diabetic patients as well as healthy controls

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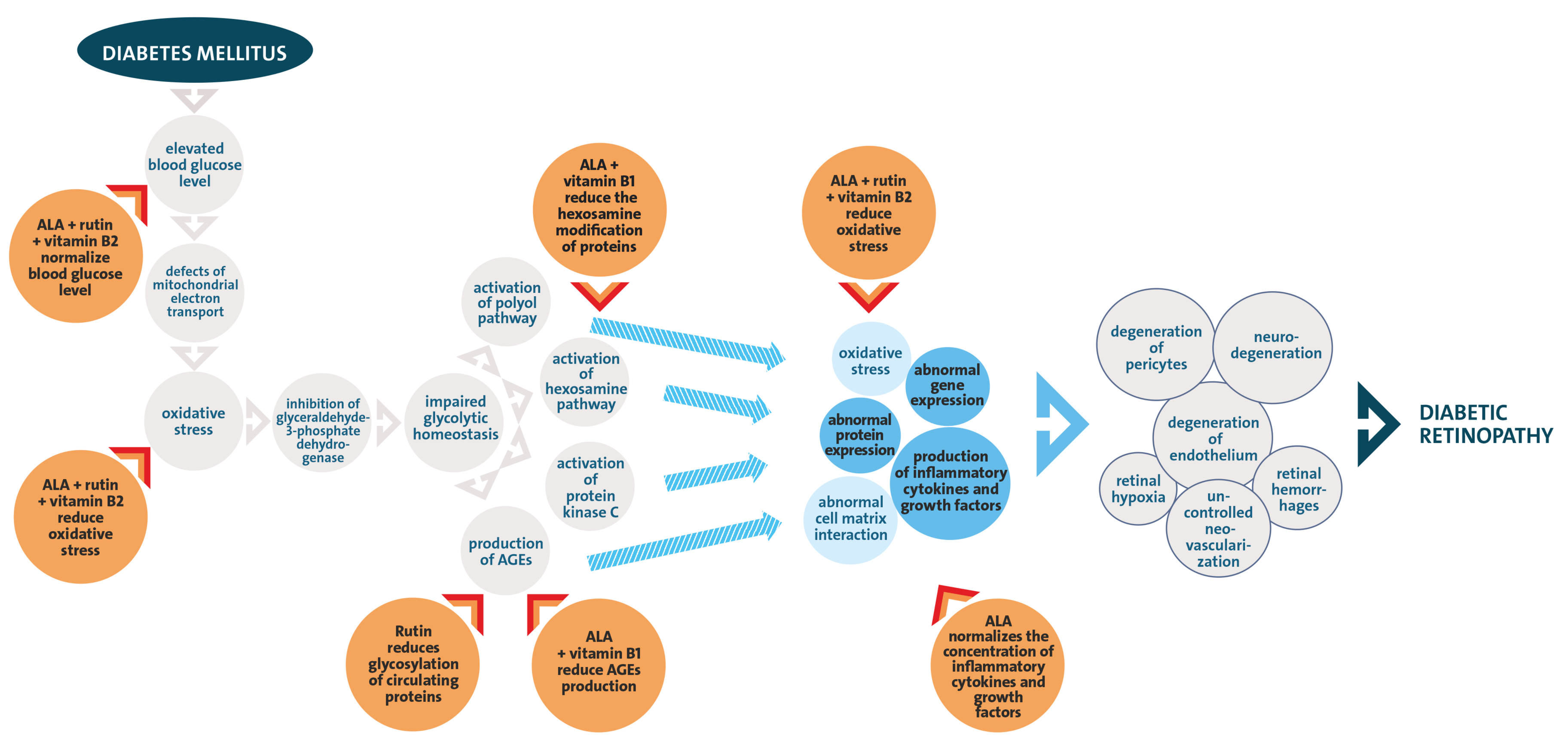
PURPOSE

To investigate the combined effect of antioxidant and antiglycating micronutrients in diabetic retinopathy (DR), a case-controlled study was conducted.
The main study parameter was contrast sensitivity (CS), since reduced contrast sensitivity is an early symptom of functional retinal dysfunction in DM patients.

INTRODUCTION

Pathogenesis of DR – hyperglycaemia induced oxidative stress



Diabetes mellitus (DM) is the leading cause of blindness in developed countries, with diabetic retinopathy (DR) being the most serious complication that can lead to vision loss. The complex pathogenesis of DR arises from hyperglycaemia-induced oxidative stress (OS) affecting capillary endothelial cells, as well as nervous and glial cells in the retina. Increased OS triggers the polyol pathway, enhances the formation of advanced glycation end products (AGEs), activates protein kinase C, and increases hexosamine pathway flux. The activation of these pathways further amplifies OS and promotes the production of inflammatory cytokines and growth factors, resulting in vascular abnormalities and increased apoptosis. Certain micronutrients may help counteract the complex pathogenesis of DR. Alpha-lipoic acid (ALA) has been shown to reduce oxidative stress and help regulate blood sugar. In combination with benfotiamine, ALA also reduces AGE formation and hexosamine modification of proteins. Additionally, supplementation with vitamin B2 and rutin has been found to lower oxidative stress and improve glucose homeostasis.

STUDY DESIGN

136 participants					
46 Type 1 diabetes		51 Type 2 diabetes		39 Healthy controls	
with supplement **44 eyes**	without supplement **45 eyes**	with supplement **43 eyes**	without supplement **45 eyes**	with supplement **39 eyes**	without supplement **38 eyes**

examination of contrast sensitivity by FACT

5 spatial frequencies (1.5, 3, 6,12 and 18 cycles per degree [cpd])
4 luminal conditions (photopic and mesopic, both with and without glare)

baseline → 3 months → 6 months

statistical analysis & evaluation of effect size

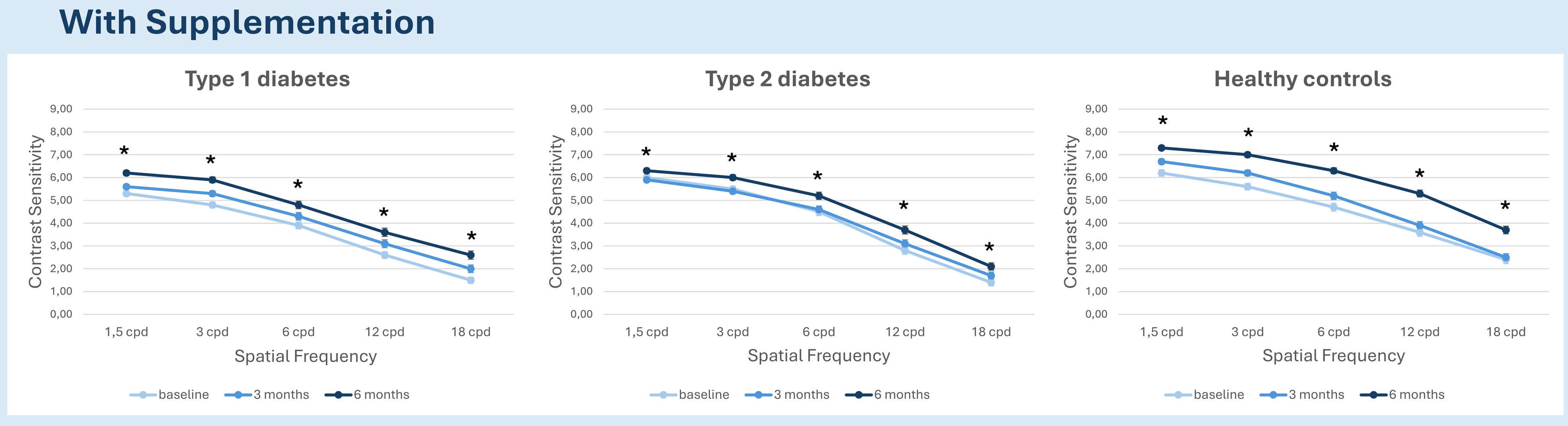
A total of 136 people participated in this case-controlled study: 46 patients with type 1 diabetes (DM1), 51 patients with type 2 diabetes (DM2), and 39 healthy controls. Participants in each group were randomly assigned to receive either one capsule daily of a food supplement containing 150 mg of R-alpha lipoic acid (R-ALA), 1.1 mg of vitamin B1, 1.4 mg of vitamin B2, and 25 mg of rutin for six months, or no supplement.
Contrast sensitivity was evaluated at baseline, and again after 3 and 6 months, using the Functional Acuity Contrast Test (FACT, Stereo Optical). In this test, each step of contrast-level change (0-9) corresponds to 0.15 log contrast sensitivity (logCS). CS was measured in each eye at five spatial frequencies (1.5, 3, 6, 12, and 18 cycles per degree [cpd]) under four different luminance conditions: photopic and mesopic, both with and without glare.
Statistically significant differences of CS at different timepoints were analysed using ANOVA/Kruskal-Wallis test as applicable. Effect size for 6 months supplementation was calculated using Cohen's d metric.

RESULTS I

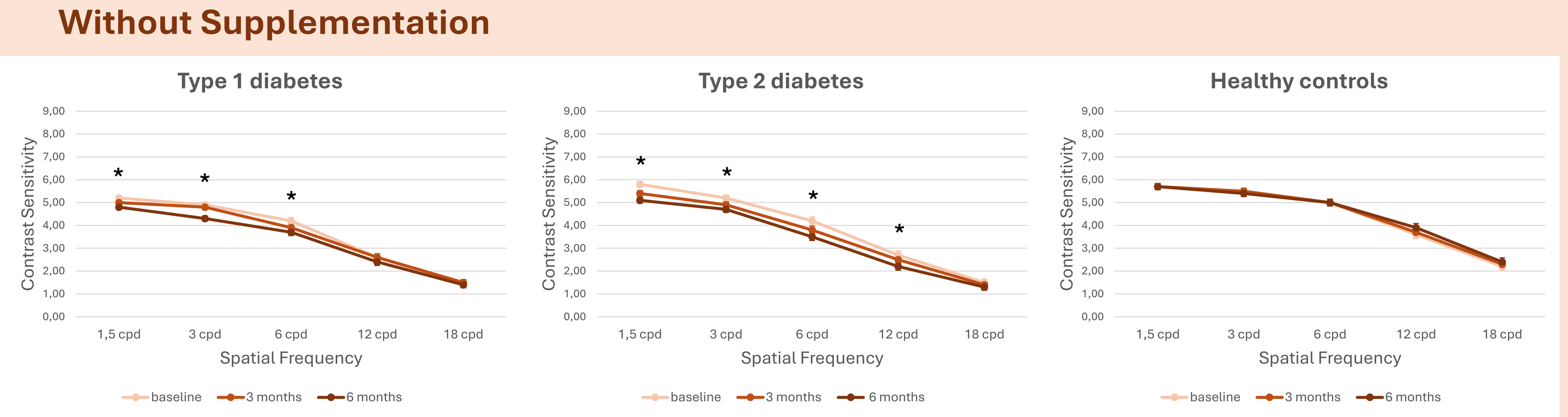
Supplementation led to significant improved contrast sensitivity

Over the six-month study period, all supplemented groups experienced a statistically significant improvement in contrast sensitivity across all spatial frequencies. In contrast, non-supplemented DM1 patients showed a decrease in contrast sensitivity at spatial frequencies of 1.5, 3, and 6 cpd. Similarly, DM2 patients who did not receive nutritional supplements exhibited a decline in contrast sensitivity at spatial frequencies ranging from 1.5 to 12 cpd. In the non-supplemented control group, contrast sensitivity remained stable throughout the study period.

With Supplementation



Without Supplementation

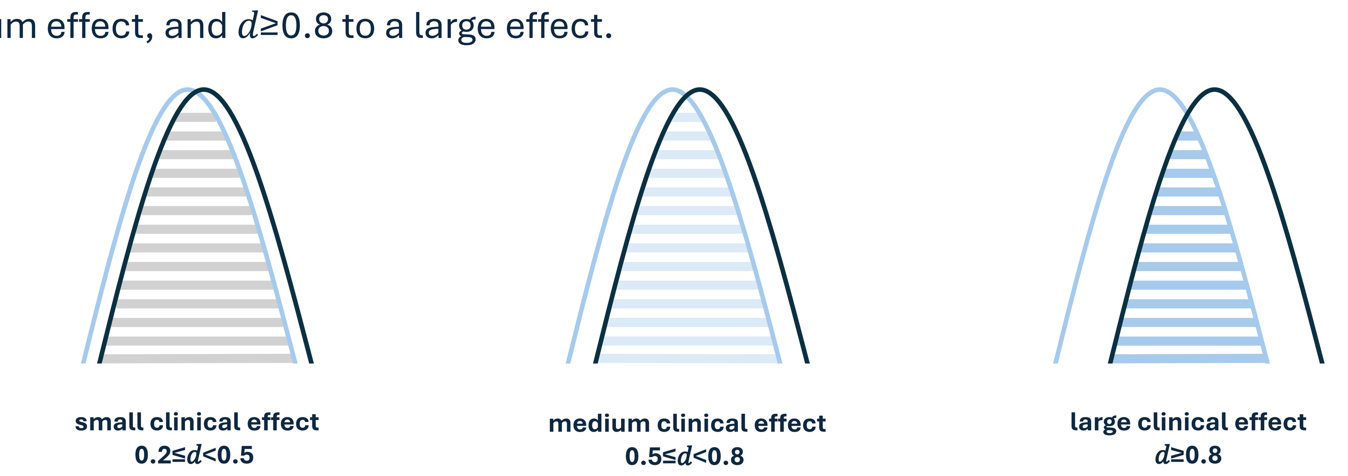


The graphs display the means and standard errors of contrast sensitivity (CS) measurements using the Functional Acuity Contrast Test (FACT). Each step of contrast-level change (0–9) corresponds to 0.15 log contrast sensitivity (logCS). An asterisk (*) indicates statistically significant differences between time points (p<0.001).

RESULTS II

Six months supplementation has a moderate effect on CS of DM1

While statistical significance measures the reproducibility of results (typically at 95% confidence level), effect size helps determine the clinical relevance of an observed effect. The effect size d can be calculated using the Cohen's d metric, where $0.2 \leq d < 0.5$ corresponds to a small clinical effect, $0.5 \leq d < 0.8$ to a medium effect, and $d \geq 0.8$ to a large effect.



To assess the clinical relevance of the micronutrient supplement for patients, the effect size was calculated for all supplemented groups.

Spatial Frequence	Effect size d		
	Type 1 diabetes	Type 2 diabetes	Healthy controls
1.5 cpd	0.580	0.193	0.611
3 cpd	0.647	0.313	0.778
6 cpd	0.428	0.318	0.727
12 cpd	0.453	0.409	0.773
18 cpd	0.471	0.350	0.591

This analysis revealed a medium effect for type 1 diabetics, a small effect for type 2 diabetics, and a medium to large effect for the healthy control group for the antioxidant/glycating micronutrient supplement studied.

CONCLUSION

In light of the study results presented, a micronutrient supplement containing alpha-lipoic acid, vitamin B1, vitamin B2, and rutin may be considered for the nutritional management of diabetics, particularly those with type 1 diabetes. Patients with type 2 diabetes may also benefit from improved contrast vision with appropriate supplementation. However, it remains to be investigated whether a similar effect size can be achieved in DM2 patients over a longer supplementation period, as observed in DM1. Additionally, the results suggest that this specific nutritional supplement could be of interest to non-diabetics experiencing reduced contrast sensitivity.

Potential conflicts of interests of presenting author: 1. no, 2. ebiga-VISION GmbH, 3. no, 4. no, 5. no, 6. no, 7. no

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