Diabetic macular edema (DME) has multifactorial and interconnected pathophysiological mechanisms, with poor glycemic control considered of major importance. Hyperglycemia, endothelial dysfunction, retinal hypoxia and oxidative stress, local inflammatory activity with upregulation of cytokines and growth factors microaneurysms, breakdown of the blood–retinal barrier, and retinal neurodegeneration have been shown to be involved in the development and progression of diabetic retinopathy. Dietary supplementation with omega-3 long-chain polyunsaturated fatty acids has emerged as one of these alternatives based on the significant role of docosahexaenoic acid (DHA), the dominant fatty acid of retinal phospholipids, in maintaining retinal integrity. The pleiotropic effects of DHA including antiinflammatory, antioxidant, antiproliferative, and antiangiogenic properties may play an important role in modulating the production of proinflammatory cytokines and proangiogenic factors, the effect of oxidative stress damage of retinal pigment epithelial cells, and the intrinsic mechanisms of other contributing pathways to endothelial vascular dysfunction in the diabetic retina. The purpose of this study is to report 3-year results of a randomized single-blind controlled trial of intravitreal ranibizumab combined with oral DHA supplementation versus ranibizumab alone in patients with DME. Patients were randomized using a table of random numbers to intravitreal ranibizumab either with oral DHA supplementation (intervention group) or without oral DHA supplementation (control group). There were 26 patients (31 eyes) in the DHA intervention group and 29 (38 eyes) in the control group. Ranibizumab (0.5 mg) was administered monthly for the first 4 months followed by a pro re nata (PRN) regimen. In the experimental group, patients received oral DHA supplementation (1050 mg/day) (Brudyretina 1.5 g). The improvement was defined as a gain of 5 or more ETDRS letters of best-corrected visual acuity (BCVA) and/or a 100 mm decrease in central subfield macular thickness (CSMT) measurement by optical coherence tomography as compared to the previous visit. Either Chi-square test or Fisher’s exact test was used for the comparison of categorical variables between the study groups. Mixed linear model analysis was used to assess differences in BCVA, CSMT, and HbA1c levels between the study groups throughout the 34-month study period. A total of 69 eyes (DHA-supplementation group 31 eyes, 26 patients; control group 38 eyes, 29 patients) were finally included and followed over 36 months. There were 35 men and 25 women (DHA group – 17 men and 9 women; control group –18 men and 11 women) with a mean age of 67.2 ± 7.6 years. In the DHA-supplementation group, the mean CSMT at the baseline of 444 ± 98 mm decreased to 301 ± 67 mm at 24 months and 275 ± 50 mm at 36 months. In controls, the mean CSMT at the baseline was 450 ± 112 mm and 345 ± 108 mm at 24 months and 310 ± 97 mm at 36 months. At 36 months, the mean decrease of CSMT was higher in the DHA-supplementation group than in controls (275 ± 50 mm vs. 310 ± 97 mm) with significant differences at months 25, 30, 33, and 34. Between-group differences in BCVA were not found, but the percentages of ETDRS gains 0.5 and 0.10 letters were higher in the DHA-supplementation group. Differences in serum HbA1c, plasma total antioxidant capacity values, erythrocyte DHA content, and serum IL-6 levels were all significant in favor of the DHA-supplementation group. There were no statistically significant differences in the number of intravitreal injections at each time interval between patients in the DHA-supplementation group and controls. DHA has an inhibitory effect on the activation of NF-kB, which is responsible for the synthesis and inflammatory cytokines and vascular adhesion molecules as well as the synthesis of metalloproteinases and VEGF, a crucial proangiogenic factor driving retinal neovascularization. Limitations of the study include the small sample size, the single-blind design, and the lack of control over dietary intake. Strengths of the study include the 3-year follow-up period and the fact that only four patients were lost between 24 and 36 months, leaving a reasonable number of patients for full evaluation at 36 months. In conclusion, in patients with DME with indication for intravitreal ranibizumab therapy, the addition of a dietary supplement rich in DHA plus antioxidant vitamins, minerals, and xanthophylls was effective to achieve better-sustained improvement of CSMT outcome after 3 years of follow-up as compared with intravitreal ranibizumab alone.
UVEAL EFFUSION SYNDROME IN 104 EYES: RESPONSE TO CORTICOSTEROIDS – THE 2017 AXEL C. HANSEN LECTURE

Shields CL, Roelofs K, Di Nicola M, Sioufi K, Mashayekhi A, Shields JA, et al. Uveal effusion syndrome in 104 eyes: Response to corticosteroids – The 2017 Axel C. Hansen Lecture. Indian J Ophthalmol 2017;65:1093-104.

Uveal effusion syndrome (UES) was first reported by Schepens and Brockhurst in a seminal paper in 1963 in which they described the clinical features in 17 male patients who demonstrated choroidal detachment, often with secondary retinal detachment, optic disc swelling, and minimal signs of uveitis. They noted that UES was “insidiously progressive over a period varying between several months (up to) 7 or 8 years.” Several theories on the pathophysiology of UES have been speculated, including vortex vein obstruction, increased choroidal permeability, intrinsic choroidal alterations, and decreased scleral permeability of which latter has been supported by histopathological studies. There are several inflammatory and hydrostatic conditions that can result in uveal effusion, but the term “UES” is reserved specifically for idiopathic cases. Based on the literature, therapy for UES generally involves surgical creation of scleral windows to decompress suprachoroidal fluid, and more recently, implantation of express valve. The mechanism of corticosteroids for UES is unclear, but some speculate that there could be generalized reduction in inflammatory factors or control of transudation and edema by membrane stabilization.

The purpose of this study was to investigate the role of corticosteroids for UES. A review of the computerized coding for patients evaluated on the Ocular Oncology Service at Wills Eye Hospital between October 1, 1975, and January 1, 2017, with the diagnosis of idiopathic UES, was retrospectively performed. Eyes classified as idiopathic UES demonstrated serous uveal detachment, with axial length >19 mm (nonnanophthalmic, Type 3), and no evident inflammatory, vascular, or tumor-related condition and normal scleral appearance and thickness by ultrasonography and/or magnetic resonance imaging (MRI). The patient demographic and clinical features were evaluated, and therapeutic intervention was recorded. Institutional review board approval was obtained. Specific treatment strategies were evaluated including primary treatment (oral, periocular, or topical corticosteroids [TCSs] or observation [OBS]) and secondary treatment (additional oral, periocular, or TCS, intravitreal corticosteroid, or surgical sclerectomy [scleral window]). Treatment outcomes were evaluated for patients who maintained follow-up in our clinic regarding VA (improvement [≥2 Snellen lines increase], stable, and worsening [≥2 Snellen lines decrease]), UES outcomes including UES any response, complete resolution, worsening, and recurrence. There were 104 eyes of 97 patients with idiopathic UES included in this analysis, and all were classified as Type 3, based on the lack of nanophthalmos and lack of scleral wall abnormality. The mean age was 70 years (median: 71, range: 27–94 years); majority were Caucasian (92%), male (64%), and with unilateral findings (87%). The referring diagnosis was choroidal melanoma (47%), choroidal metastasis (3%), choroidal tumor nonspecified (34%), and UES (16%). The chief complaints included decreased vision or visual field (VF) loss (56%), pain (11%), other symptoms (19%), or no symptoms (14%). The therapeutic intervention included OBS (n = 54, 52%), oral corticosteroids (OCS) (n = 27, 26%), PCS (n = 12, 12%), and TCS (n = 11, 11%). In general, eyes receiving OCS, PCS, and TCS showed more advanced features than those treated with OBS. Compared to eyes managed with OBS, those treated with OCS (vs. OBS) demonstrated higher rate of associated retinal detachment (59% vs. 31%, P = 0.029), those treated with PCS (vs. OBS) showed poorer initial VA of 20/20–20/40 (0% vs. 30%) and higher rate of associated retinal detachment (100% vs. 31%, P < 0.001), and those treated with TCS (vs. OBS) showed poorer initial VA of 20/200–20/400 (45% vs. 15%, P = 0.034). Overall, the median time to effusion response was 3 months and to complete resolution was 11 months. In the entire group of 59 eyes, only three (5%) needed scleral window surgery (2 following OCS and 1 following PCS). Regarding complications, cataract was more commonly found in OCS versus OBS (33% vs. 5%, P = 0.044). There was no case of corticosteroid-induced glaucoma. A more recent review on 19 eyes with UES suggested classification into three groups based on axial length and scleral thickness, including Type 1 (nanophthalmic eye, axial length <19 mm), Type 2 (nonnanophthalmic eye with abnormal thickened sclera documented on MRI), and Type 3 (nonnanophthalmic eye without scleral abnormality).[3] These authors found that sclerectomy was effective for Types 1 and 2, but not Type 3. They commented that Type 3 had no detectable abnormality, classified as truly “idiopathic” and represented two cases (11%) in their series, both with no effect from surgical sclerectomy and eventuating in VA of hand motions and 20/200. In our study, we specifically evaluated Type 3 UES in nonnanophthalmic eyes and with normal sclera by ultrasonor or MRI. We found that corticosteroids were beneficial for eyes with more advanced features, worse initial VA, or more extensive serous retinal detachment, and those with less advanced disease were managed conservatively with OBS, often with spontaneous resolution. In summary, oral, periocular, topical, or a combination of corticosteroids can be considered for therapy of UES, in the absence of...
nanophthalmos and/or scleral thickness abnormalities. In this series, corticosteroids provided control of UES in 95% of cases. If control is not achieved, then consideration for scleral window surgery is an option.

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**Conflicts of interest**
There are no conflicts of interest.

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