

Antioxidant treatment of Smith-Lemli-Opitz syndrome (SLOS) and retina function determined by electroretinography

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Introduction

Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive disease caused by a defect in cholesterol metabolism, resulting in elevated 7-dehydrocholesterol (7DHC) and progressive retinal degeneration.

SLOS may be mild, moderate or severe based on serum levels of cholesterol, 7DHC and clinical characteristics.

Phototransduction is abnormal in SLOS, likely due to high levels of 7DHC in cell membranes of photoreceptors, free radical formation and retina cell death.

Cholesterol and antioxidant supplementation may protect against SLOS retinopathy.^{1,2,3}

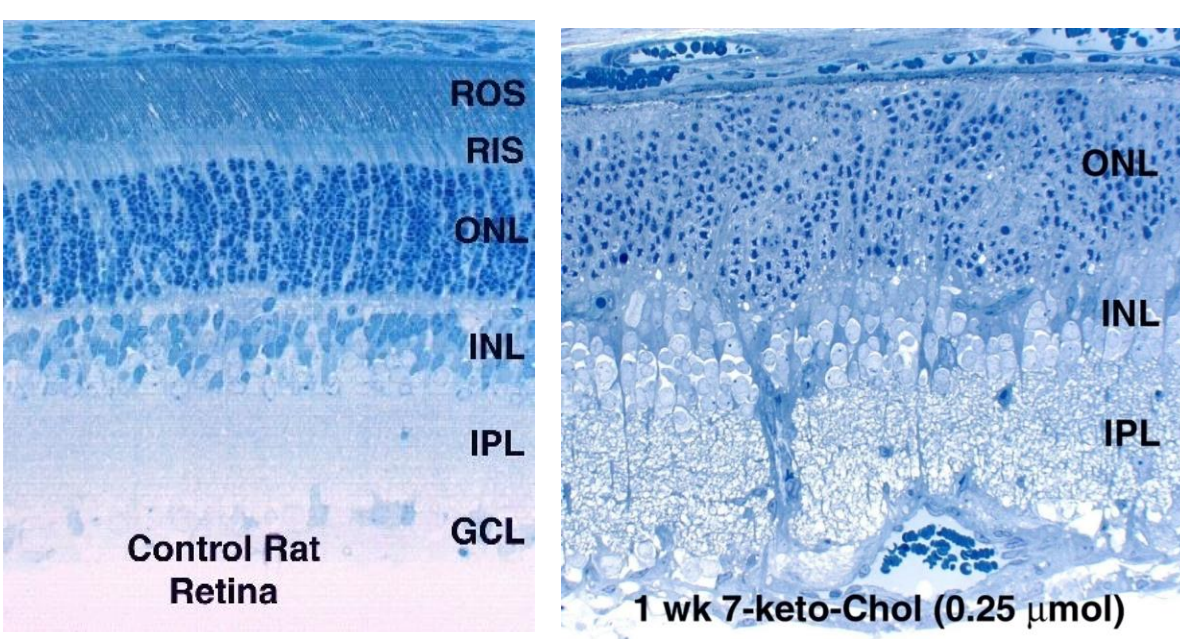


Figure 1. Effects of oxysterols on rat retina, with control on left and oxysterol injection on right.⁴

Purpose

The purpose of this study was to determine the effect of treatment with cholesterol and antioxidant/vitamin (DEKAS Plus and AQUADEKS) supplementation on the retina function in patients with SLOS by electroretinography (ERG).

Methods

IRB approval was obtained prior to conducting the study.

9 Patients with SLOS were prospectively enrolled.

Data presented is from 2008-2022.

2008 – present patients were treated with cholesterol and Antioxidants- first AQUADEKS, and more recently DEKAS Plus via liquid or capsule.

Cholesterol supplementation was adjusted based on patient body weight and 7DHC levels

Supplement Facts

Serving size: 1 softgel • Servings/container: 60

	Amount per softgel	% DV*
Calories	5	
Total Vitamin A (as 92% beta-carotene and 8% palmitate)	18,167 IU	363
Vitamin C (as sodium ascorbate)	75 mg	125
Vitamin D3 (as cholecalciferol)	800 IU	200
Vitamin E (as d-alpha-tocopherol)	150 IU	300
Vitamin K1 (as phytylquinone)	700 mcg	875
Thiamin (as thiamin mononitrate)	1.5 mg	100
Riboflavin (Vitamin B2)	1.7 mg	100
Niacin (as niacinamide)	10 mg	50
Vitamin B6 (pyridoxine HCl)	1.5 mg	95
Folic Acid	200 mcg	50
Vitamin B12 (as cyanocobalamin)	12 mcg	200
Biotin	100 mcg	33
Pantothenic Acid (as calcium D-pantothenate)	12 mg	120
Zinc (as zinc sulfate)	10 mg	67
Selenium (as selenomethionine)	75 mcg	107
Sodium	10 mg	<1
Vitamin E (as other mixed tocopherols)	80 mg	*
Coenzyme Q10	10 mg	*

*Daily value not established for these nutrients



Figure 2. DEKAS Plus nutritional information⁵

Nutritional Information

softgels	DEKAS Plus	capsules	DEKAS Essential	capsules	DEKAS Plus
One pack contains	60 softgels	60 capsules	60 capsules	60 capsules	60 softgels
Vitamin A	18,167 IU	18,167 IU	18,167 IU	18,167 IU	18,167 IU
Vitamin C	75 mg	75 mg	75 mg	75 mg	75 mg
Vitamin D3	800 IU	800 IU	800 IU	800 IU	800 IU
Vitamin E	150 IU	150 IU	150 IU	150 IU	150 IU
Vitamin K	700 mcg	700 mcg	700 mcg	700 mcg	700 mcg
Thiamin	1.5 mg	1.5 mg	1.5 mg	1.5 mg	1.5 mg
Riboflavin	1.7 mg	1.7 mg	1.7 mg	1.7 mg	1.7 mg
Niacin	10 mg	10 mg	10 mg	10 mg	10 mg
Vitamin B6	1.5 mg	1.5 mg	1.5 mg	1.5 mg	1.5 mg
Folic Acid	200 mcg	200 mcg	200 mcg	200 mcg	200 mcg
Vitamin B12	12 mcg	12 mcg	12 mcg	12 mcg	12 mcg
Biotin	100 mcg	100 mcg	100 mcg	100 mcg	100 mcg
Pantothenic Acid	12 mg	12 mg	12 mg	12 mg	12 mg
Zinc	10 mg	10 mg	10 mg	10 mg	10 mg
Selenium	75 mcg	75 mcg	75 mcg	75 mcg	75 mcg
Sodium	10 mg	10 mg	10 mg	10 mg	10 mg
Vitamin E (other mixed tocopherols)	80 mg	80 mg	80 mg	80 mg	80 mg
Coenzyme Q10	10 mg	10 mg	10 mg	10 mg	10 mg



Figure 3. DEKAS Plus nutritional information⁵

A baseline ERG under anesthesia was performed according to ISCEV standards when possible.

Repeat ERG's were performed a minimum of one year after initiating treatment.

Results

Table 1. Classifications of enrolled patients.

	Sex	Age at most recent Electroretinogram (years)	Classification
Patient 1	M	14	Moderate
Patient 2*	M	58	N/A
Patient 3	M	20	Mild
Patient 4	M	29	Mild
Patient 5	M	29	Mild
Patient 6	M	27	Severe
Patient 7	M	12	Moderate
Patient 8	F	15	Moderate
Patient 9	F	4	Moderate

*Patient 2 was excluded from this data analysis due to limited ERG result availability

Table 2. Cholesterol averages and ranges of patients in Mild, Moderate, and Severe Cohorts at time of first ERG.

	Mild n=3	Moderate n=4	Severe n=1
Serum Cholesterol	146.6666667 (98-195)	139 (102-165)	64
Serum 7-DHC	3.043333333 (1.37-6)	3.5 (1.9-6.2)	8.1
Serum 8-DHC	1.706666667 (0-3.9)	4.775 (2.4-8.4)	6.8
Sterol Ratio %	2.972326304 (1.197-5.077)	5.731983703 (3.333-8.848)	23.28

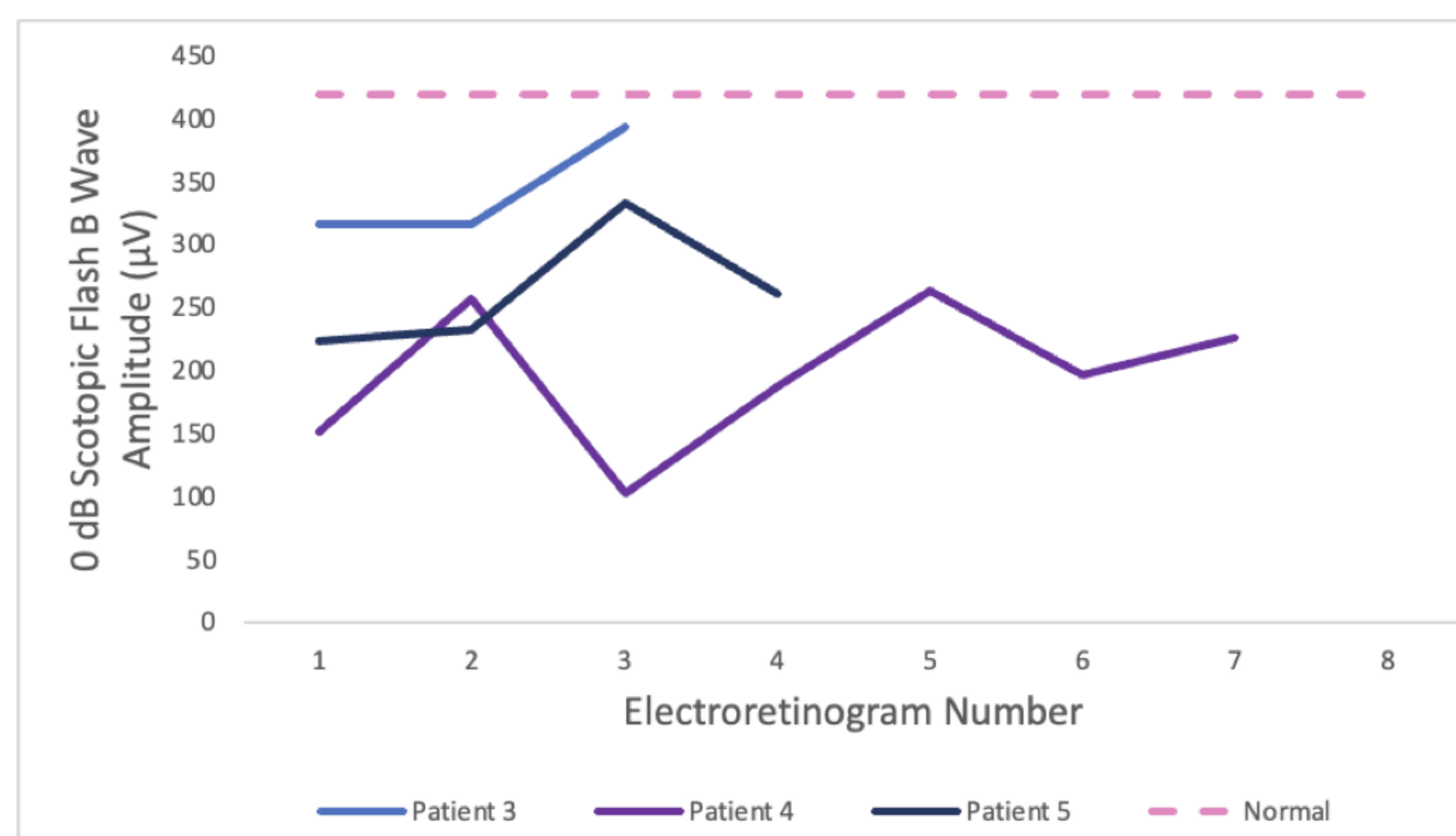


Figure 4. 0 dB Scotopic Flash B wave amplitude over time for patients in Mild cohort.

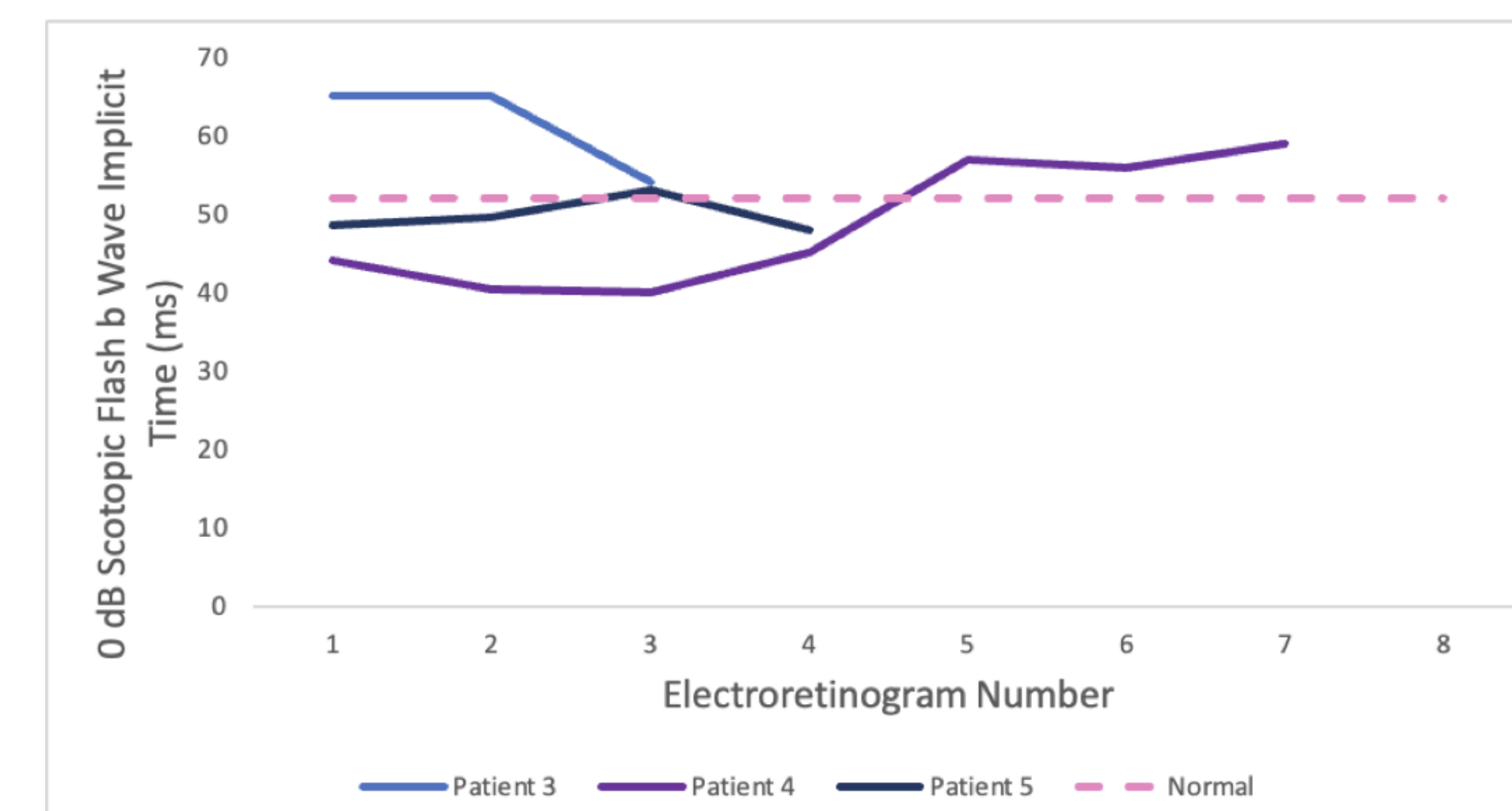


Figure 5. 0 dB Scotopic Flash B wave implicit time over time for patients in Mild cohort. It should be noted that findings less than 52 ms are normal values.

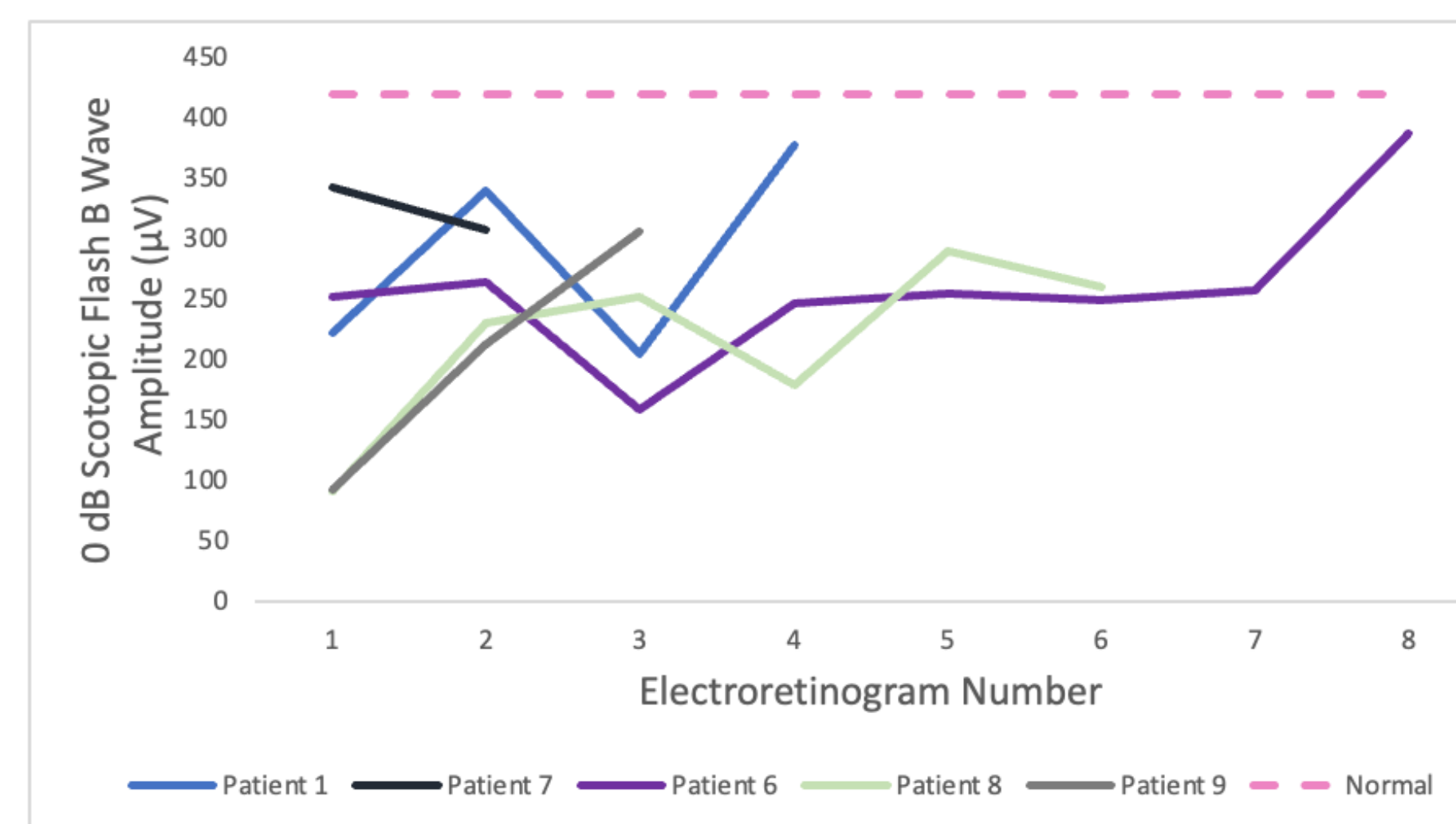


Figure 6. 0 dB Scotopic Flash B wave amplitude over time for patients in Moderate and Severe cohort.

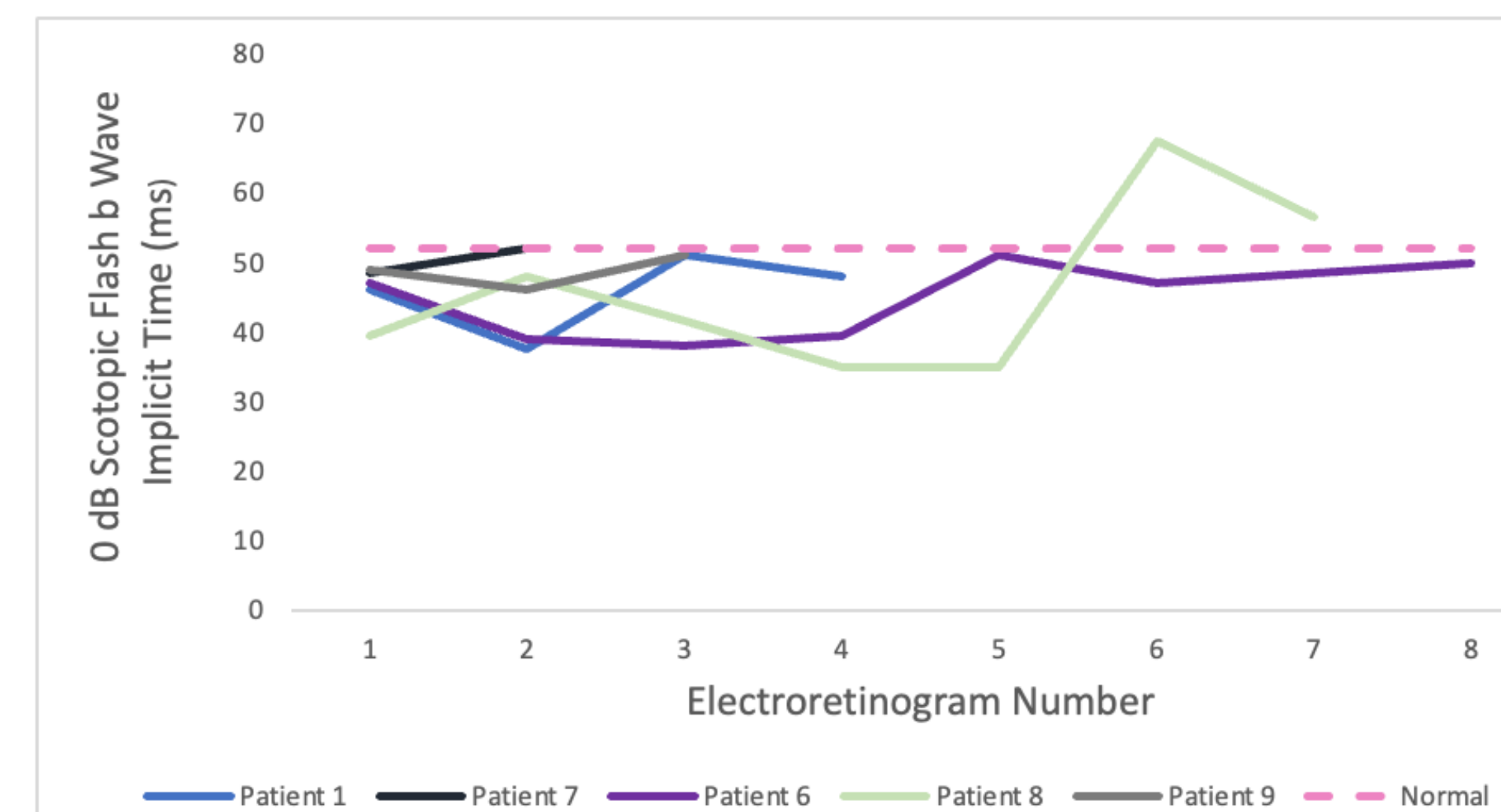


Figure 7. 0 dB Scotopic Flash B wave implicit time over time for patients in Moderate and Severe cohort. It should be noted that findings less than 52 ms are normal values.

In Mild patients:

- There were decreased amplitudes, but rods improved towards normal values (Figure 4)
- Increased implicit time improved in 2 of 3 patients but remained mildly abnormal (Figure 5)

In Moderate patients:

- Decreased amplitudes improved from moderate to mild towards normal values in 3 of 4 patients (Figure 6)
- Implicit times remained within normal ranges in 3 of 4 patients (Figure 7)

In Severe patient:

- There were mild to moderate decreased amplitudes in rods which improved over time (Figure 6)
- Implicit times remained within a normal range (Figure 7)

Discussion

This study allows us to objectively follow retinal function for patients with a known degenerative pigment retinopathy

Over time as patients continue to take antioxidants there is a stabilization if not an improvement in rod function.

Future research is needed to determine which particular antioxidants are most impactful and the most optimal doses.

Future studies will analyze oxysterol levels to see if antioxidants help decrease levels of oxysterols and their damaging effects.

Conclusions

Treatment of SLOS with cholesterol and antioxidants is associated with improvement of retina function determined by electroretinography.

Further study of antioxidants and retina function may someday help treat other diseases that result in retinal degeneration.

Literature Cited

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The authors have no financial or proprietary interest in any of the material presented. Support by The Pediatric Clinical Translational Research Center at the Children's Hospital Colorado and Colorado Clinical and Translational Sciences Institute Grant number UL1RR025780.